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Assistant Physician and Demonstrator of Practical Medicine, St. Bartholomew's Hospital; Physician, Royal Chest Hospital; Consulting Physician, Royal National Sanatorium, Bournemouth

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By Gwenvron M. Griffiths, M.D., M.R.C.P. Lond.
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J. Tylor Fox, M.A., M.D. Camb., D.P.M.
MEDICAL SUPERINTENDENT OF THE COLONY

ANY attempt to define epilepsy stresses the tendency of epileptic phenomena to recur as one of its most important characteristics. The circumstances governing recurrence are often as little understood as the causation of the original fit. It is a matter of common observation that in some cases fits occur only during the night, or about the time of rising, or during the day; some patients have their fits singly, others in groups with varying intervals of freedom.

It seemed to us worth while to make a study of the fit incidence in a number of patients over long periods, and to note the effect of drugs and other factors upon it. Charts were made of the fits of 110 boys and men at the Lingfield Epileptic Colony, showing the time of day and type of every fit over a considerable period, in some cases as long as 10 years. These charts, together with four womens' charts chosen to demonstrate some special feature, form the basis of this paper.

The fits recorded include all major attacks, and minor attacks involving loss of consciousness with or without partial convulsion. Except in cases where they are indicated, attacks of automatism, absences, localised or general myoclonus or other manifestations that come under the rather loose heading of petit mal are not included.

LONG-DISTANCE RHYTHM

A study of the charts shows that many patients have fits, either singly or in groups, at regular intervals. The most striking case is that of a boy who, for three successive years, had an isolated fit in the month of March. In the fourth year he had an attack of status epilepticus in March and died in a few hours. We have found no other case to parallel this.

Two sisters at Lingfield show unusual long-distance rhythms that are curiously alike. In the elder sister (Fig. 1) there is a cycle of about two years, with diminishing free intervals. The regularity of the cycle is disturbed by the onset of menstruation in 1936. In the younger, the cycle shown on the chart (Fig. 2) is somewhat shorter, but was evidently preceded by a longer cycle before admission. In neither case did medication appear to have any influence on the number or grouping of the fits.

The most easily understood rhythm is the monthly or menstrual rhythm, a typical case of which is shown in Fig. 3, where fits spread over a week or so follow the onset of the menstrual period. But this monthly rhythm is not confined to women. In Figs. 4, 5, and 6 we show examples of equally regular monthly rhythm in three males, aged respectively 11, 20, and 40.

But several cases show rhythms that have no known physiological counterpart.

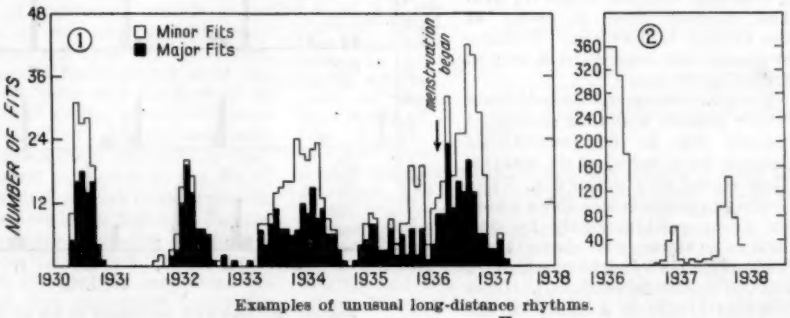
Thus in Fig. 7 there are fit recurrences every 3½ months, in Fig. 8 every 7 weeks, and in Fig. 9 every 5 weeks. Fig. 10 shows the record of a patient who for many years had fits for a month and was clear the next, an example of an unusual 2-monthly rhythm. Shorter rhythms can also be found. Fig. 11 shows a 3-weekly rhythm, and Figs. 12 and 13 fairly regular fortnightly rhythms.

We have not discovered any seasonal rhythms in this series unless it be the first case referred to of fits only in the month of March, nor any lunar or weekly rhythms. The cases referred to so far have all shown periods of freedom between rhythmically spaced fits, or groups of fits, but other cases with frequent fits at short intervals show regular rhythmic increases and decreases in the number of the attacks.

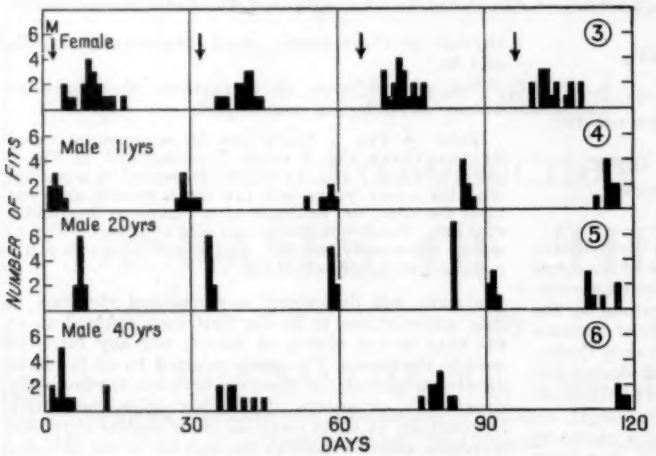
These long-distance rhythms are usually resistant to drugs. The number of fits in a group may be diminished, but the grouping remains. In two of the cases mentioned above there was a free interval of over a year, followed by the reappearance of fits in the same rhythm as before.

We must conclude that these rhythms are inherent or constitutional. It is possible that they are intimately associated with neurological dysfunction underlying the epileptic manifestations, but it seems more reasonable to think of them as metabolic or endocrine in origin, as is clearly the case with the monthly rhythm. These metabolic or endocrine rhythms take no share in the causation of the epilepsy, but are probably effective in determining the occurrence of fits in an epileptic.

The absence of any case showing weekly rhythms seems to us of considerable significance. It is well recognised that environmental factors often play a part in the determination of fits in patients who are liable to them. Fear, anxiety, or boredom encourage fits, while new interests or pleasurable excitement inhibit them. A patient admitted to hospital for observation of his attacks often fails to produce the desired phenomena. Now institution life is, even more than normal community life, routine in nature. It has two principal periodicities, the daily, of which we shall write later, and the weekly. For children the weekly routine includes five days' school, a day off, a Sunday with services, set nights for entertainments, scouts, guides, and so on, and for adults, a similar routine with two free half-days in the week. In such a routine there must be high lights and low



Examples of unusual long-distance rhythms.



Examples of monthly rhythm.

lights, popular and unpopular events. If environmental factors play any rôle in determining the fits one would expect that in some at least of our patients a weekly rhythm would appear on the charts. The absence of any example of weekly rhythm strengthens the view that epilepsy is much more influenced by inherent factors, be they neurological, metabolic, or circulatory, than by emotional states dependent on the environment. This view is supported by a study of the hourly incidence of fits.

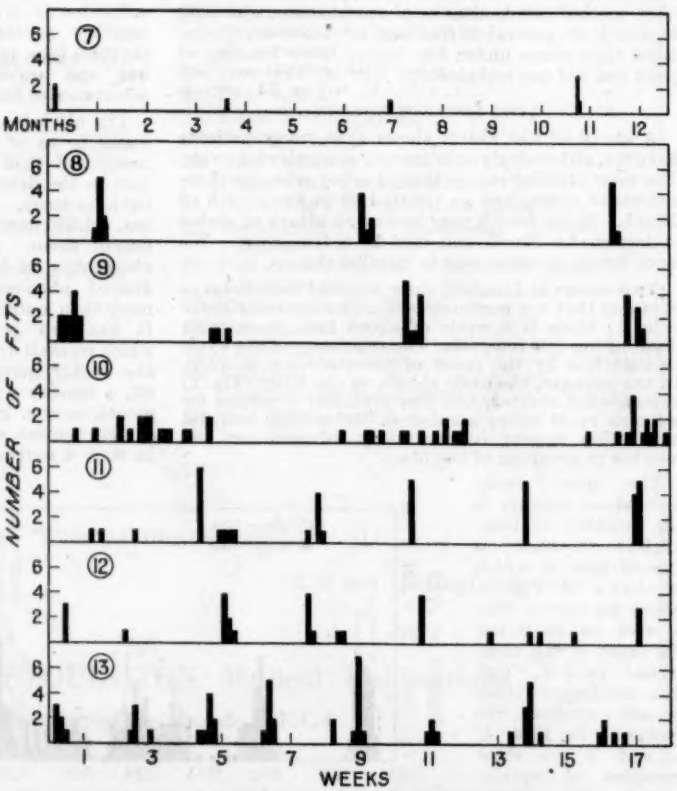
TIME OF DAY

The consideration of the time of day of fits shows that many epileptics have a predilection for certain times for their fits. If we lump together all the fits, both major and minor, in all the 110 patients studied in this series (39,929 fits) we find that by far the greatest incidence is at 6–7 A.M., there being a steady rise from 3 A.M. to this peak and a very abrupt fall at 8 A.M. (Fig. 14). The next most popular time for fits is between 10 P.M. and midnight. There is a smaller peak from 11 A.M. to noon, the last hour of school, and the time immediately before the midday meal. The lowest incidences are between 5 and 9 P.M. and between 9 and 11 A.M. The average time of rising at the Colony is 6.30 A.M. Bedtime is spread out from 7 to 9.30 P.M. according to age.

Langdon-Down and Russell Brain (1929) publish a similar picture of massed fits in 66 institutional patients for a period of six months. They record only major fits. They divide the patients into those whose fits occur predominantly by day (diurnal), those who have them predominantly by night (nocturnal), and the remainder (diffused). Helen Hopkins (1933) in a study of the time incidence of fits in 302 non-institutional cases divides the fits into diurnal, nocturnal, and "awakening," limiting the latter period to the first hour after arousal. In view of the very high peak between 5 and 8 A.M. and the number of patients we have found who have fits predominantly between those hours, it seems to us wise to distinguish a special rising group.

Classified in this way 104 of our cases showed that 40 are predominantly "night fitters," 39 are predominantly "day fitters," 11 are predominantly "rising fitters," and 14 are "diffused." In parentheses, it may be noted that the rising fitters are a particularly intelligent group, and that most of the patients whose fits usually occur in the afternoon are low-grade or deteriorating cases. If we add together all the fits during the 10 bedtime hours of 9 P.M.–7 A.M. (19,918) they almost exactly equal those that occur during the remaining 14 hours (20,011).

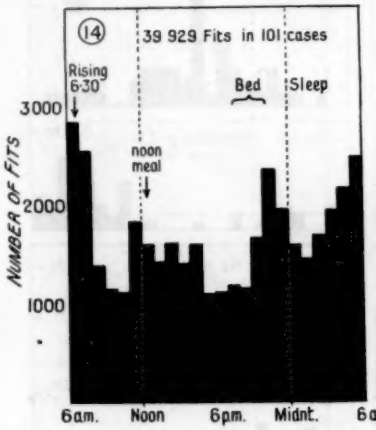
We agree with Magnussen (1936) that sleep is probably the most important factor in the determination of peak times. According to their reaction to this factor, patients tend to have fits during the early part of the night when sleep is deepest, during the latter hours of the night in the transition period



Regular rhythms with recurrence of fits at various intervals.

from sleeping to waking, within an hour of the time of rising at the end of sleep, or during the day when sleep is absent.

The gradually ascending incidence from 3 A.M. onwards, which reaches its peak at 8 A.M. and then drops suddenly, extends well beyond the time of rising. Denny-Brown and Graeme Robertson (1934) have pointed out the slow fall of cerebro-spinal fluid pressure that marks the transition from the sleeping to the waking state and may encourage the onset of fits, but fits after rising need some different explanation. The assumption of the erect position has been suggested; but patients do not commonly have attacks immediately after getting out of bed, as one would expect if posture were an important factor.



Incidence of fits according to time of day.

The rising peak occurs at a time furthest away from the last meal, and it is tempting to regard this peak and that between 11 A.M. and noon as due to hypoglycæmia associated with starvation. But observations by one of us (G. M. G.) on 24 cases in this series failed to disclose any early morning hypoglycæmia, and Lennox (1927) in a study of 267 patients found that blood-sugar content has no relation to fits.

Some of our most consistent night fitters show an occasional lapse into an afternoon attack which turns out on investigation to have happened during a Sunday afternoon nap. In this connexion, too, we may refer to the interesting case of a patient who was moved from a junior home where he went to bed at 8.30 P.M. to a senior one where he retired an hour later. As will be seen from Fig. 15 his peak time moved on exactly an hour with the change.

Our massed chart (Fig. 14) should only be taken as giving a very general indication of peak times. The periods of recorded fits vary for different patients, and those with very large numbers of fits will of course exercise a preponderating influence on the form of the chart. Moreover, as we shall see later, drugs may greatly influence the time incidence of fits, and, in any case, the study of individual records is far more instructive. Thus, if we take patients who have fits in series and chart out their time incidence, we often find the fits spread fairly evenly over the 24 hours. If, however, we take only the first fit of a series, and fits that occur singly, a very different picture is almost always obtained. The fits are really not diffused at all but have a clear and definite peak time, and it would be sound to regard all the fits of a series subsequent to the first as part of the epileptic manifestation that started with the first fit. For the purposes of studying the time incidence all the fits except the first should be disregarded. This is well brought out in Figs. 16–21. In the last case, the series always starts with two successive major fits at 11 P.M. and 2 A.M. followed by a few attacks of epileptic automatism spread out over the next few days (see Fig. 22).

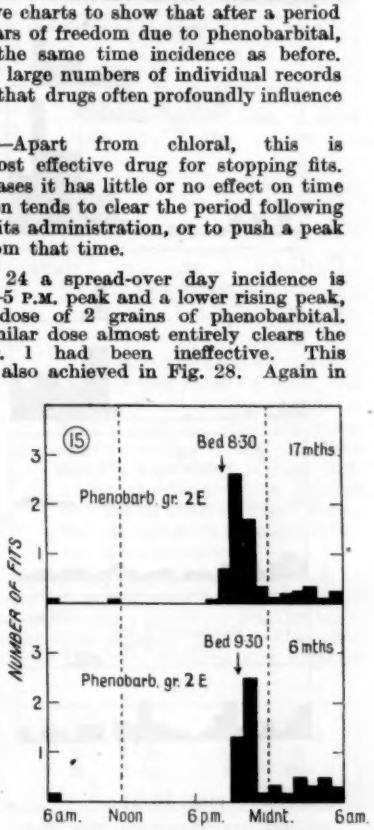
Further study of the time incidence of the first fit in patients with series of fits led to the discovery, in a few cases, of a very peculiar phenomenon, a "herald" fit 2–5 days before the series proper begins. This herald fit usually has a definite hour incidence of its own; and it looks as if, in the cases in which it occurs, we must conceive of an epileptic manifestation or unit of epileptic activity beginning with the herald fit, and finishing with the last fit of the series (see Fig. 23).

EFFECT OF DRUGS ON THE TIME INCIDENCE OF FITS

Langdon-Down and Russell Brain (1929) concluded that sedative drugs have no influence on the time incidence of fits. While some of the fits are suppressed, the peaks remain the same. This is often true, and we have charts to show that after a period of months or years of freedom due to phenobarbital, fits recur with the same time incidence as before. An inspection of large numbers of individual records shows, however, that drugs often profoundly influence time incidence.

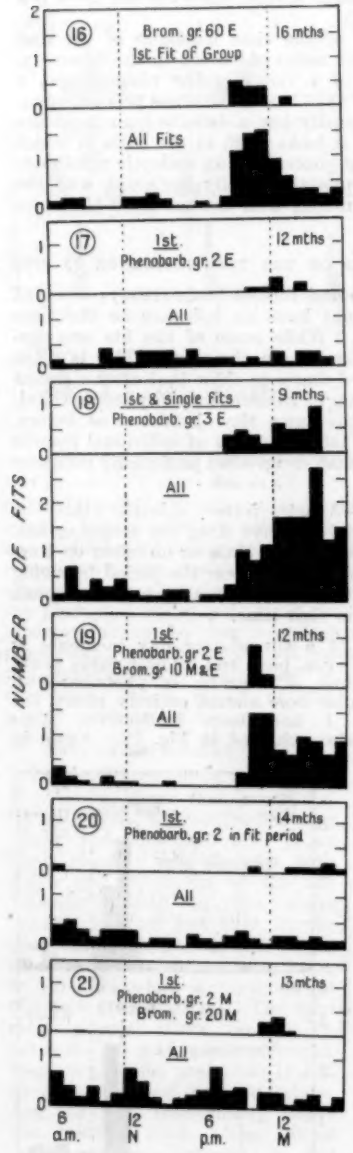
Phenobarbital.—Apart from chloral, this is probably the most effective drug for stopping fits. While in some cases it has little or no effect on time incidence, it often tends to clear the period following immediately on its administration, or to push a peak further away from that time.

Thus in Fig. 24 a spread-over day incidence is pushed into a 4–5 P.M. peak and a lower rising peak, by a morning dose of 2 grains of phenobarbital. In Fig. 26 a similar dose almost entirely clears the day, where gr. 1 had been ineffective. This happy result is also achieved in Fig. 28. Again in Fig. 25 we see a predominantly day fitter converted into a predominantly night fitter by a morning dose, and in Figs. 27 and 29 fits that were strictly confined to the day are spread out over the 24 hours. Similar effects are shown in Figs. 30 and 31. In Fig. 32 we see that with gr. 2 in the morning the patient has fits spread over the 24 hours, with a peak in the later hours of the night. When the dose is changed to the evening, the patient is clear till midnight, has a low late-night incidence, and most of his fits occur in the day. In Fig. 33 gr. 1 of phenobarbital morning and evening results in fits spread out fairly evenly over the 24 hours. When gr. 2 is given only in the morning, the day is partly cleared and the night fits are increased. Dramatic effects are seen in Figs. 34, 36, and 38, where a dose



Effect of a change of bedtime.

In this and subsequent charts of this type each abscissa covers a 24-hour period, starting at 6 A.M. The ordinates represent the average number of fits per month during the period stated in each case.



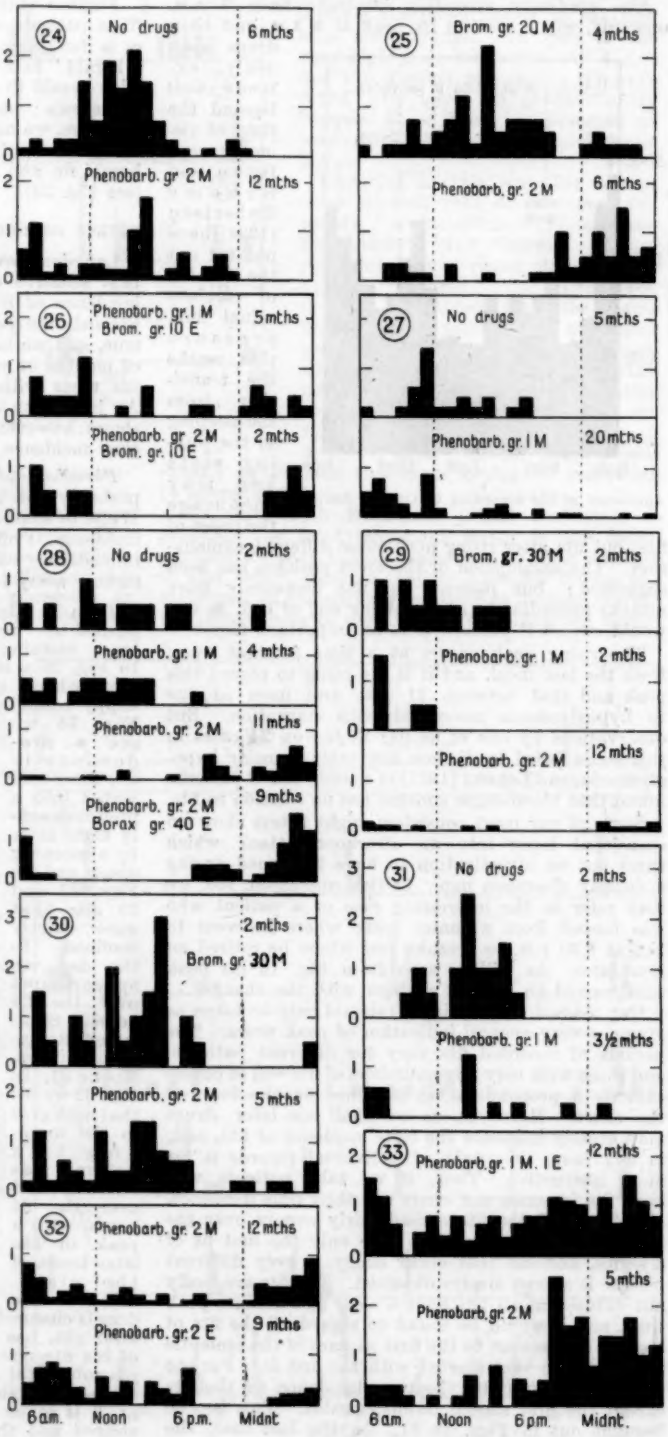
FIGS. 16–21:

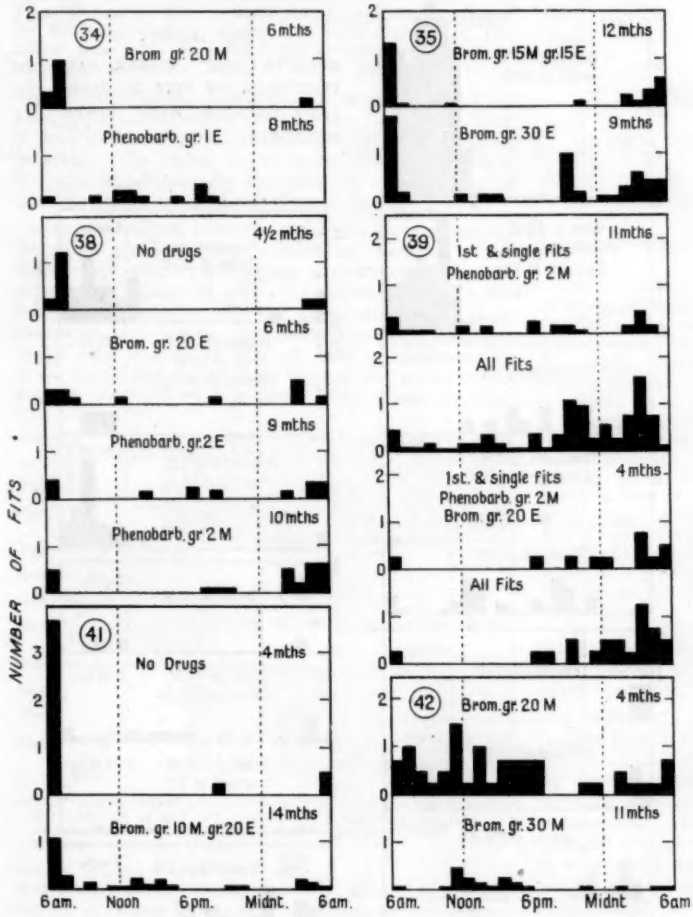
CHARTS ILLUSTRATING THE FALLACY OF RECORDING ALL THE FITS OF PATIENTS WHO HAVE THEM IN SERIES. THE TRUE TIME INCIDENCE IS OBTAINED ONLY BY CONFINING THE RECORD TO THE FIRST FIT OF EACH SERIES AND THOSE THAT OCCUR SINGLY.

(See legend to Fig. 15.)

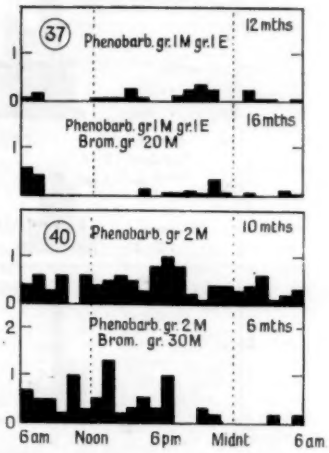
M = morning E = evening

FIGS. 24–33: EFFECTS OF PHENOBARBITAL ON INCIDENCE OF FITS





FIGS. 34, 35, & 37–42: EFFECTS OF PHENOBARBITAL AND OF BROMIDE ON THE INCIDENCE OF FITS.

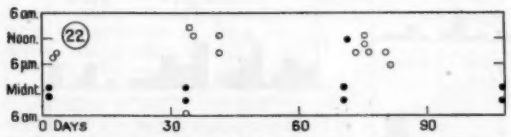


of phenobarbital spreads consistently rising fits over the day.

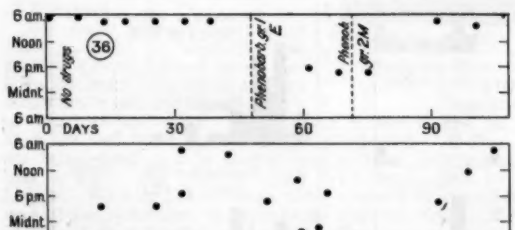
These and other charts show clearly that phenobarbital acts promptly, and in clinical work it is very important to give it just before the time when fits are expected.

Bromide has been very widely used in this series of cases, but a survey of the records shows that it does not often affect the time incidence of fits. In those cases where there is clear evidence of alteration, it appears to have its greatest effect during the second twelve hours after its administration.

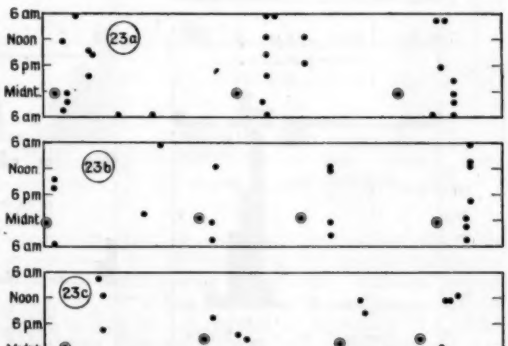
Thus, in Fig. 39 the addition of an evening dose of bromide clears the day of fits, while in Figs. 40 and 42 a morning dose clears the night. In Fig. 35 more fits occur at night with a single evening dose than when half the dose is given morning and evening.



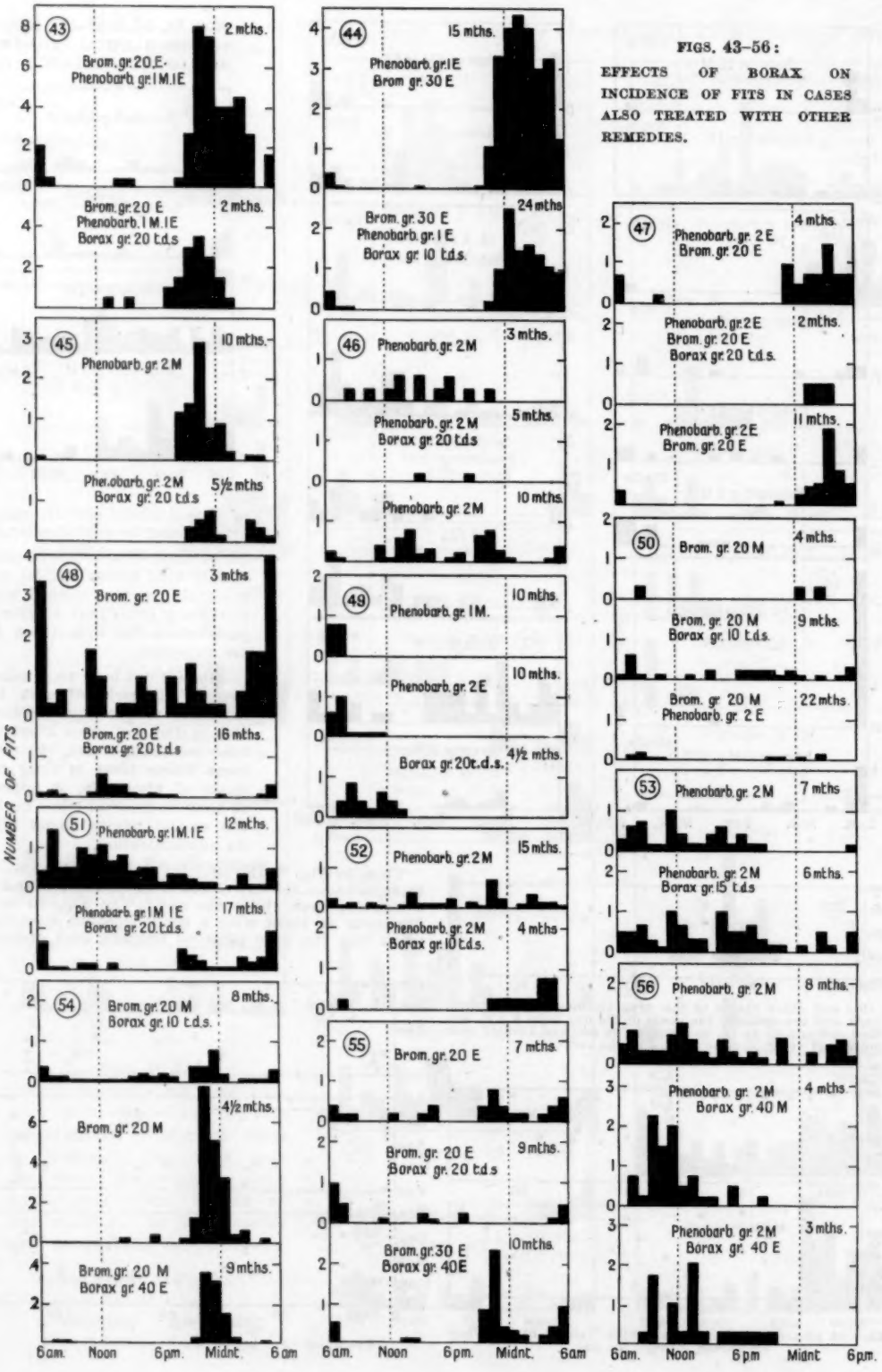
In this and other charts of this type the abscissa represents days and the ordinate the hours of the day from 6 A.M. and then downwards to 6 A.M. again. The day and hour of each individual fit is therefore located on the chart.



Effect of phenobarbital in a case with "rising fits." They are spread through the day.



Examples of "herald fits" (encircled dots).


NUMBER OF FITS
(43) 2 mths. Brom. gr. 20 E. Phenobarb. gr. 1 M. 1 E
Brom. gr. 20 E Phenobarb. 1 M. 1 E Borax gr. 20 t.d.s 2 mths.
(44) 15 mths. Phenobarb. gr. 1 E Brom. gr. 30 E
Brom. gr. 30 E Phenobarb. gr. 1 E Borax gr. 10 t.d.s. 24 mths.
(45) 10 mths. Phenobarb. gr. 2 M
Phenobarb. gr. 2 M Borax gr. 20 t.d.s 5½ mths.
(46) Phenobarb. gr. 2 M 3 mths.
Phenobarb. gr. 2 M Borax gr. 20 t.d.s 5 mths.
Phenobarb. gr. 2 M 10 mths.
(47) Phenobarb. gr. 2 E Brom. gr. 20 E 4 mths.
Phenobarb. gr. 2 E Brom. gr. 20 E Borax gr. 20 t.d.s. 2 mths.
Phenobarb. gr. 2 E Brom. gr. 20 E 11 mths.
(48) Brom. gr. 20 E 3 mths
Brom. gr. 20 E Borax gr. 20 t.d.s 16 mths.
(49) Phenobarb. gr. 1 M. 10 mths.
Phenobarb. gr. 2 E 10 mths.
Borax gr. 20 t.d.s. 4½ mths.
(50) Brom. gr. 20 M 4 mths.
Brom. gr. 20 M Borax gr. 10 t.d.s. 9 mths.
Brom. gr. 20 M Phenobarb. gr. 2 E 22 mths.
(51) Phenobarb. gr. 1 M. 1 E 12 mths.
Phenobarb. gr. 1 M 1 E Borax gr. 20 t.d.s. 17 mths.
(52) Phenobarb. gr. 2 M 15 mths.
Phenobarb. gr. 2 M Borax gr. 10 t.d.s. 4 mths
(53) Phenobarb. gr. 2 M 7 mths
Phenobarb. gr. 2 M Borax gr. 15 t.d.s 6 mths.
(54) Brom. gr. 20 M Borax gr. 10 t.d.s. 8 mths.
Brom. gr. 20 M 4½ mths.
Brom. gr. 20 M Borax gr. 40 E 9 mths.
(55) Brom. gr. 20 E 7 mths.
Brom. gr. 20 E Borax gr. 20 t.d.s 9 mths.
Brom. gr. 30 E Borax gr. 40 E 10 mths.
(56) Phenobarb. gr. 2 M 8 mths.
Phenobarb. gr. 2 M Borax gr. 40 M 4 mths
Phenobarb gr. 2 M Borax gr. 40 E 3 mths.
6 am. Noon 6 pm. Midnt. 6 am
6 am. Noon 6 pm. Midnt. 6 am
6 am. Noon 6 pm Midnt 6 pm.

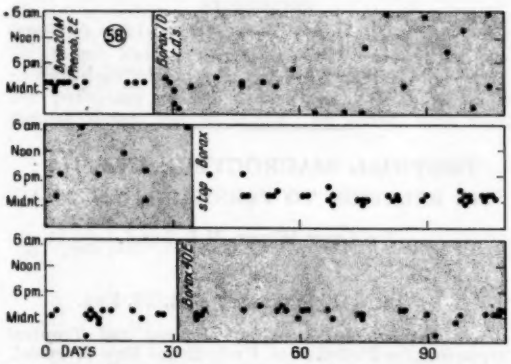
FIGS. 43–56:

EFFECTS OF BORAX ON INCIDENCE OF FITS IN CASES ALSO TREATED WITH OTHER REMEDIES.

On the other hand in Fig. 37 we see a morning dose clearing the 8 hours immediately succeeding. In Figs. 38 and 41 very definite rising peaks are replaced by fits scattered over the day and night. In the latter case the immediate disturbance of the time incidence is clearly brought out in Fig. 57 B.

The consideration, however, of large numbers of bromide records leaves us with the impression that it does not matter much what time of day the drug is given. Its value in stopping fits is not very likely to be affected by the relation of the time of administration to the peak time of the fits.

Borax.—Sodium biborate is a much more uncertain drug than phenobarbital or bromide. But it is sometimes very effective, causing a dramatic reduction or even stoppage of fits. In other cases the fits increase in number. In the doses used here, toxic symptoms are occasionally seen, the most common being skin lesions or loss of hair. Unfortunately these toxic symptoms may appear in cases whose fits are lessened by the drug. The effect on time

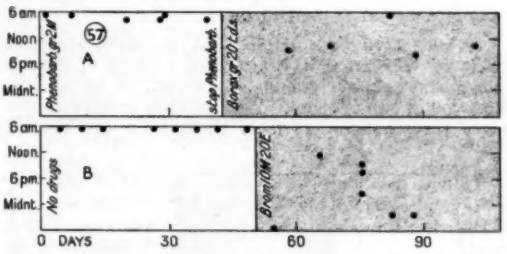


In this case the effect of borax (first stippled area) was to reduce the number of fits but scatter them through the day. An evening dose (second stippled area) reduced the number without scattering them.

incidence is most erratic, and it is difficult to see any rhyme or reason in the results obtained.

The usual plan was to give borax in doses of gr. 10 or 20 three times a day. Five charts (Figs. 43–47) show considerable reduction of fits on this type of dosage with preservation of time incidence. In another case (Fig. 48) there is also a great reduction in fits, associated with the disappearance of serial fits and the abolition of a well-marked rising peak. In Fig. 51 a predominantly day fitter is converted into a night fitter, a similar result being seen in Fig. 52, where a diffused fitter has his day cleared of fits.

We have already seen that phenobarbital or bromide can scatter a well-defined peak (see Figs. 36 and 57 B). This happens also with borax and is well shown in Figs. 49 and 57 A. Scattering is also shown in Figs. 50 and 53, with a considerable increase of fits. An interesting case is shown in Fig. 58. This man had a clear and definite peak with many fits at 10 P.M. With gr. 10 of borax three times a day there was some reduction in numbers, but the fits were scattered over the day and night. This was regarded as a disservice to the patient. So the borax was discontinued, and the patient regained his 10 P.M. peak with increased fits. Next a single dose of gr. 40



Scattering with borax (first stippled area) and also with bromide (second stippled area).

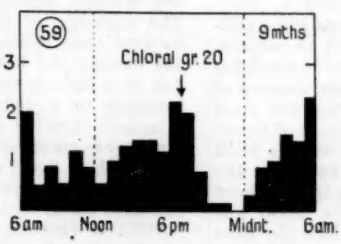
of borax at bedtime was tried. The result was satisfactory; the fits were reduced in number, but the 10 P.M. peak was maintained. We cannot pretend to explain these phenomena, but their existence as shown in Fig. 54 as well as Fig. 58 is beyond all question.

Encouraged by this case, we gave one large dose of borax at bedtime or in the morning to several other patients, but results have been inconsistent. In Fig. 55 an almost pure day fitter on gr. 20 three times a day is converted into an almost pure night fitter, on a single evening dose of gr. 40. Evening borax also clears the day in Fig. 28. In Fig. 56 a single dose of gr. 40 clears the night in a diffused fitter, but it does not make any difference if the dose is given in the morning or evening.

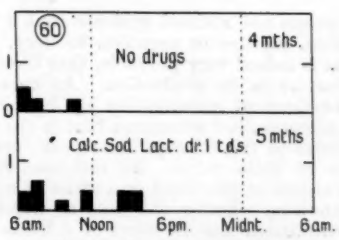
Borax is certainly a remarkable drug in epilepsy, but it seems impossible to predict its effect either on the numbers or time incidence of fits, although in some patients the effect in either case may be dramatic.

Chloral.—One man received a daily dose of gr. 20 of chloral at 7 P.M. for some time. This was justified by the fact that without it he had frequent severe attacks of status epilepticus, which the daily chloral suppressed. Without the chloral his fits were well diffused; with the chloral, as Fig. 59 shows, there is a very sharp fall in fits from 8 P.M. to 1 A.M. with almost complete absence between 9 P.M. and midnight. Chloral acts quickly and its effects are over in a few hours.

Other drugs.—For the sake of completeness, we think it well to mention that drugs, other than those



Effect of a daily dose of chloral at 7 P.M.

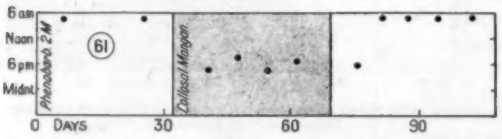


Scattering effect of calcium sodium lactate.

commonly used in epilepsy, may affect the time incidence of fits. We record a few that we have come across in looking over the records. *Calcium sodium lactate* gr. 60 three times a day scatters a definite peak in Fig. 60. A course of injections of *Collosal manganese* changes a rising time peak into a 6 P.M. peak for the duration of the treatment (Fig. 61). A dose of *mist. ferri sulph.* three times a day crowds the fits into a peak for a few months (Fig. 62).

DISCUSSION

It will have been noted that we have recorded cases in which the day has been cleared of fits by phenobarbital, by bromide, by borax, or by a combination of two of them. Most patients greatly appreciate this change. It frees them from the risk of



Effect of injections of colloid manganese (stippled area). Peak changes from hour of rising to 6 P.M.

accident and from interference with their daily occupations. By manipulation of the dosage and time of administration, we believe that many epileptics may be rendered clear of fits in the daytime.

Sufficient has been said to show that unconsidered mass records of time incidence may be misleading. This applies to the individual case, as well as to large numbers of cases aggregated together. To arrive at what we may call the inherent or constitutional time incidence of fits, the patient must be observed for a considerable time without any drugs, and in all cases with serial attacks all the fits, except the first of the series, must be discounted. With these precautions, it might well be found that most epileptics had a definite hour at which fits were most likely to occur. For in this connexion be it observed that scattering by drugs is much commoner than peaking.

The determination of such a peak hour is of more than academic significance. For it enables us to locate a definite daily rhythm in the patient. What is the nature of the rhythm? We do not know, but

Fits crowded into a peak during treatment with ferric sulphate (first stippled area).

we are not without evidence that it bears some relation, positive or negative, to sleep. Let us assume, as is indeed very probable, that there are biochemical factors in its production. An enormous volume of biochemical investigation has been carried out upon epileptics, but we suggest that in the absence of knowledge of the inherent time peak, much of this work is of little value. To estimate, for instance, the calcium in the blood of a series of epileptics, without knowing whether the time at which the blood was withdrawn was 12 hours or 6 hours before the time peak or was right in the middle of it, is we venture to think just waste of time. Biochemical estimations made soon after fits are likely to be of little value, because they may be merely expressions of metabolic processes occurring in the fit itself. Before we started this investigation we thought that the only biochemical estimations of much value were serial estimations, say every hour or two, made for a few hours immediately preceding a fit. Obtaining such serial estimations is laborious and often disappointing, for in most cases fits are difficult to predict with any certainty. With the knowledge of the inherent or constitutional time peak, however, the whole problem is made very much easier. Serial estimations covering any 24-hour period will give results of value, as we see what alterations occur in relation to the time peak. Moreover it will obviously be advantageous to choose, for research purposes, cases with clear-cut time peaks. Similar considerations apply equally to biochemical work done on patients who show long-distance rhythm.

SUMMARY

1. Consideration has been given to various forms of rhythm to be found in the fit records of a large group of epileptics.

2. Inherent rhythms, both of a "long-distance" and "time of day" type, have been found in many cases.

3. Drugs often modify the time of day rhythm profoundly.

4. The importance of inherent rhythm in biochemical and other investigations has been suggested.

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TROPICAL MACROCYTIC ANÆMIA: ITS RELATION TO PERNICIOUS ANÆMIA

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TROPICAL macrocytic anæmia has been described by various workers in different parts of the world and there is general agreement that the blood picture resembles very closely that of pernicious anæmia and those cases of sprue that develop a macrocytic anæmia. In a paper to be published shortly it will be shown that the bone-marrow picture too is very similar to that of pernicious anæmia. The ætiology of the tropical anæmia has also up to date been related to that of pernicious anæmia: the disease has been regarded as a deficiency state due to a lack in the diet of Castle's extrinsic factor, resulting in a deficiency in the body of the liver principle curative in pernicious anæmia. The fact that the tropical anæmia responded well when treated with either liver extracts or substances, such as Marmite, which are known to be good sources of the extrinsic factor lent support to this view (Wills 1934).

With a view to investigating the nature of the missing dietetic factor, presumed to be the extrinsic factor, experimental work with rhesus monkeys was undertaken. It was possible to produce in these animals by faulty feeding an anæmia considered to be the animal counterpart of the tropical anæmia (Wills and Stewart 1935). This monkey anæmia was cured by those preparations, marmite by mouth and liver extracts by both the oral and parenteral routes, which are active in the cure of the tropical condition in man. The current theory of the deficiency origin of the latter disease was therefore extended to the monkey anæmia. This was the position until

in the course of experiments with purified liver extracts it was found that the anæmic animals failed to respond to the more highly purified extracts, even in enormous doses. Anahæmin (British Drug Houses), an extract prepared by the method of Dakin and West (1935, 1936); Examen, an extract prepared by the method of Drs. Laland and Klem (1936) and kindly given us by these workers, and a similar commercial extract prepared by Glaxo Ltd.; and cruder extracts made from Campolon were tried and found inactive (Wills, Clutterbuck, and Evans 1937). These surprising results led to the present investigation of the response of the human tropical cases to such purified extracts, as it was of great practical and theoretical interest to discover if these were active in the human disease. The results of the work are reported below.

CLINICAL TRIALS

The patients studied were all suffering from a typical macrocytic anæmia (Table I) as judged by the colour-index and the mean cell volume and were all strictly comparable with those previously described (Wills and Mehta 1930, Wills 1934). Both men and women were included in the series. In another paper the pathology of the disease will be discussed in greater detail but it should be noted that most of the patients tested had normal amounts of free acid in their gastric contents, all had normal plasma bilirubin values, none had nervous lesions, and many had normal tongues, differing in these respects from any similar series of cases of pernicious anæmia.

The extracts tested were all given parenterally. In assessing the activity of a preparation both the increase in the red cell count and the height of the reticulocyte response were considered, though the significance of the latter is not always clear, especially in complicated cases.

The first preparation tested was *anahæmin* as it has had extensive clinical trials and is well known to be highly active in the cure of pernicious anæmia. The results obtained in 9 cases of the tropical anæmia and in 1 case of sprue are set out in Table II. For comparison the figures from a case of pernicious anæmia and from 2 cases of monkey anæmia similarly treated are included.

The doses used should be noted: the pernicious anæmia patient had an initial dose of 4 c.cm. of anahæmin and this dose was repeated on the tenth day; the other patients and the monkeys were treated with relatively enormous doses, varying from a maximum of 2 c.cm. daily for ten days to a minimum of 12 c.cm. in nine days. The patient with pernicious anæmia responded with a reticulocytosis of 33 per

TABLE I—CONDITION BEFORE TREATMENT

Case No.	Sex.	Age.*	Diagnosis.	R.B.C. (millions per c.mm.).	Hb. (g. %).	C.I.	M.C.V.‡ (μ^3).	Ret. (%).	W.B.C. (per c.mm.).	Bilirubin (mg. per 100 c.cm.).	Free HCl after histamine (c.cm. N/10 acid %).	Nerve lesions.	Tongue changes.
1	F.	72	PA	1·351	5·8	1·59	133	1·9	2600	0·2	–	+	a.
2	F.	27	TMA	1·026	3·2	1·15	139	0·3	2600	0·4	n.	–	–
20	M.	28	TMA	1·335	5·4	1·46	153	<0·1	2000	0·23	80	–	g.
84	M.	..	TMA	1·835	6·2	1·22	134	0·4	4000	0·4	+	–	–
66	F.	30	TMA	0·996	3·0	1·05	119	<0·1	1400	0·52	n.	–	–
92	F.	..	TMA	0·750	3·2	1·54	156	0·5	1400	0·52	n.	–	g.
70	F.	..	TMA	2·580	8·4	1·20	127	<0·1	6000	0·23	n.	–	g.
36	F.	50	Sprue.	2·040	5·8	1·02	n.	<0·1	1300	0·36	n.	–	–
122	M.	35	TMA	1·240	3·1	0·92	n.	<0·1	2300	0·32	n.	–	–
25	M.	..	TMA	0·803	3·2	1·36	152	0·5	5400	0·52	78	–	–
93	M.	25	TMA	0·895	3·1	1·18	134	0·6	3100	0·64	15	–	g.
M 7	M.	..	NMA	4·110†	9·9	0·85	83·5	0·9	9450	0·0	n.	–	..
M 45	F.	..	NMA	2·765	6·5	0·80	n.	0·5	5100	0·0	n.	–	..
2	M.	54	PA	1·736	7·1	1·44	126	0·4	2500	+	–	+	a.
23	F.	20	TMA	0·876	2·55	1·06	116	<0·1	2200	0·20	–	–	–
94	M.	28	TMA	1·307	4·9	1·34	143	0·6	3800	0·0	88	–	g.
3	F.	41	PA	1·230	4·2	1·25	n.	1·0	4000	+	–	+	g.
4	F.	59	PA	1·790	7·2	1·42	137	0·6	3400	0·80	–	+	a.
5	F.	43	PA	1·562	6·5	1·45	127	1·7	5500	0·40	–	+	a.
M 52	F.	..	NMA	3·646	7·5	0·75	n.	0·6	7300	n.	6	–	..
123	M.	45	TMA	1·000	3·1	1·12	130	0·4	2500	0·52	72	–	a.
19	F.	25	TMA	0·757	2·75	1·33	159	1·6	2400	1·04	n.	–	–
35	M.	30	TMA	1·317	5·8	1·61	170	<0·1	3400	0·36	30	–	g.
21	M.	35	TMA	0·855	3·0	1·29	140	1·9	6400	0·26	112	–	–
119	M.	40	TMA	0·945	3·6	1·40	153	<0·1	3800	0·32	–	–	–

* Age of all Indian patients approximate only. † For normal figures for monkeys see Wills and Stewart (1935).
‡ M.C.V. = mean corpuscular volume.
+ = presence of. – = absence of. n. = no test done. a. = atrophic changes. g. = glossitis.
PA = pernicious anæmia; TMA = tropical macrocytic anæmia; NMA = nutritional macrocytic anæmia of monkeys.

TABLE II—RESPONSE TO ANAHÆMIN AND OTHER LIVER EXTRACTS

Diagnosis, Case No., and sex.	Period of treatment.	Treatment given.	Effect on R.B.C.* and ret.† after 1 to 10 or more days of treatment.‡														
				—	−	0	1	2	3	4	5	6	7	8	9	10	−	−
PA§ 1 ♀	1st	Anahæmin, 4 c.cm. on days 0 and 10.	R.B.C.	..	1·665 (−7)	1·351	..	..	..	..	1·778	..	..	..	..	2·625	3·460 (19)¶	..
			Ret.	..	2·8	2·5	2·1	3·1	8·1	27·0	33·0	31·2	14·6	7·2	6·0	7·0	0·4	..
			Rise or fall.‖	..	..	..	..	..	..	..	..	..	..	..	..	+ 1·274	+ 2·109	..
TMA 2 ♀	1st	Anahæmin, 2 c.cm. alternate days for 10 days.	R.B.C.	..	..	1·230	..	..	..	..	1·090	..	..	..	..	1·026	..	..
			Ret.	..	..	0·3	0·6	0·1	2·5	2·1	0·9	0·1	1·6	2·7	0·1	0·3	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	− 0·204	..	..
	2nd	$(NH_4)_2SO_4$ insoluble fraction campolon, 2 c.cm. daily for 10 days.	R.B.C.	..	..	1·026	..	..	..	..	0·994	..	..	..	..	1·180	..	..
			Ret.	..	..	2·7	2·9	3·2	1·5	3·2	3·1	4·8	2·8	0·7	−	−	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	+ 0·154	..	..
	3rd	$(NH_4)_2SO_4$ soluble fraction campolon, 4 c.cm. alternate days for 10 days.	R.B.C.	..	..	1·180	..	1·130	..	..	..	..	2·42	..	..	..	2·805 (11)	3·020 (18)
			Ret.	..	..	−	3·2	2·6	7·4	9·5	16·4	4·2	3·2	2·5	−	−	−	−
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	..	+ 1·625	+ 1·840
TMA 20 ♂	1st	Anahæmin, 2 c.cm. daily for 12 days.	R.B.C.	..	1·335 (−2)	1·335	..	..	..	..	1·305	..	..	..	..	1·383	..	..
			Ret.	..	..	< 0·1	< 0·1	0·7	< 0·1	< 0·1	< 0·1	< 0·1	0·5	1·0	1·0	< 0·1	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	+ 0·048	..	..
	2nd	Campolon, 2 c.cm. daily for 10 days.	R.B.C.	..	..	1·383	..	..	..	..	1·547	..	..	..	..	2·135	3·110 (18)	..
			Ret.	..	..	< 0·1	2·4	0·6	4·3	5·8	15·9	13·9	11·1	−	6·4	1·2	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	+ 0·752	+ 1·727	..
TMA 84 ♂	1st	Anahæmin, 2 c.cm. daily for 10 days.	R.B.C.	..	..	1·835	..	..	..	..	1·465	..	..	..	..	1·655	1·595 (14)	..
			Ret.	0·4	(−7)	0·9	1·3	2·2	1·5	1·0	2·4	2·5	2·1	2·3	1·3	1·3	0·2	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	− 0·180	0·240	..
	2nd	Liver filtrate factor, 2 c.cm. alternate days for 10 days.	R.B.C.	..	..	1·595	..	..	..	..	1·930	..	..	..	..	1·935	..	..
			Ret.	..	..	0·2	0·4	0·2	0·2	< 0·1	0·8	2·4	5·8	1·3	1·2	2·3	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	+ 0·340	..	..
	3rd	Neo-Hepatex, 4 c.cm. alternate days for 10 days.	R.B.C.	..	..	1·935	..	..	..	..	2·097	..	..	..	2·540	..	..	3·342 (15)
			Ret.	..	..	3·5	2·1	1·6	0·5	8·0	3·3	3·9	3·5	0·4	6·0	3·5	2·3 (11)	—
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	+ 0·605	..	..	+ 1·407
TMA 66 ♀	1st	Anahæmin, 10 c.cm. in 5 days.	R.B.C.	..	..	0·996	..	..	..	..	0·876	..	..	..	..	..	0·892 (11)	1·080 (18)
			Ret.	..	..	< 0·1	< 0·1	< 0·1	1·1	1·2	6·0	2·1	< 0·1	0·4	—	4·4	3·6	4·8
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	..	− 0·104	+ 0·084
	2nd	Neo-Hepatex, 14 c.cm. in 7 days.	R.B.C.	..	..	1·080	..	..	..	..	1·382	..	..	..	..	2·036	..	..
			Ret.	..	..	4·8	0·8	2·6	0·4	0·9	3·8	8·5	2·3	0·5	3·0	1·5	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	+ 0·956	..	..
TMA 92 ♀	1st	Anahæmin, 2 c.cm., and liver filtrate factor, 2 c.cm., alternate days for for 11 days.	R.B.C.	..	..	0·750	..	..	0·750	..	..	..	..	0·730	..	..	0·700 (11)	..
			Ret.	..	..	< 0·1	0·5	1·2	1·6	0·2	0·3	0·8	0·1	0·1	0·3	1·8	0·3	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	− 0·020	..	..	− 0·050	..
	2nd	Chappell's liver extract, 1·5 c.cm. alternate days for 11 days: five injections, 5 c.cm. patient's blood.	R.B.C.	..	..	0·700	..	..	..	..	..	0·760	..	..	..	1·432	1·792 (17)	2·259 (28)
			Ret.	..	..	0·3	1·0	1·7	1·7	−	6·1	11·0	10·3	6·0	5·2	3·1	< 0·1	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	+ 0·732	+ 1·092	+ 1·559

TABLE II—RESPONSE TO ANAHÆMIN AND OTHER LIVER EXTRACTS—(*continued*)

Diagnosis, Case No., and sex.	Period of treatment.	Treatment given.	Effect on R.B.C.* and ret.† after 1 to 10 or more days of treatment.‡														
			—	—	0	1	2	3	4	5	6	7	8	9	10	—	—
TMA 70 ♀	1st	Anahæmin, 2 c.cm. daily for 5 days.	R.B.C.	..	2·580	..	..	..	..	..	1·970	..	..	..	2·130	2·035 (14)	..
			Ret.	..	< 0·1	..	..	..	..	..	1·2	1·4	—	0·7	0·7	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	— 0·450	— 0·545	..
	2nd	Special Pernaemon preparation, 2 c.cm. daily for 10 days.	R.B.C.	..	2·035	..	..	..	..	..	1·970	..	..	..	1·950	..	..
			Ret.	..	..	0·3	1·0	0·8	—	—	< 0·1	—	0·3	0·1	0·1	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	— 0·085	..	..
	3rd	Neo-Hepatex, 2 c.cm. daily for 10 days.	R.B.C.	..	1·950	..	..	..	..	1·977	..	..	..	..	2·445	..	..
			Ret.	..	0·1	—	0·5	0·2	0·4	0·4	2·2	2·5	4·7	5·5	3·4	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	+ 0·495	..	..
Sprue 36 ♀	1st	Anahæmin, 4 c.cm. alternate days for 3 doses.	R.B.C.	..	2·040	..	..	..	..	1·900	..	..	..	..	2·170	1·730 (16)	..
			Ret.	..	—	..	..	..	..	1·0	..	..	..	..	< 0·1	0·9	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	+ 0·130	— 0·310	..
	2nd	Campolon irregular; 12 c.cm. in 17 days, 22 c.cm. in 25 days.	R.B.C.	..	1·730	..	..	..	..	..	..	2·070	..	..	2·190	3·360 (42)	..
			Ret.	..	0·9	..	..	..	..	..	..	..	..	..	..	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	+ 0·460	+ 1·630	..
TMA 122 ♂	1st	Anahæmin, 4 c.cm. daily for 5 days.	R.B.C.	..	1·240	..	..	..	..	1·465	..	..	..	..	..	..	..
			Ret.	..	< 0·1	< 0·1	1·0	1·0	< 0·1	**20·4**	2·3	1·0	2·3	0·9	Died	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	..	..
TMA 25 ♂	1st	Anahæmin, 2 c.cm. daily for 10 days.	R.B.C.	..	0·803	..	..	●	..	0·900	..	..	..	..	..	1·170 (11)	1·875 (15)
			Ret.	..	< 0·1	0·5	0·8	0·7	1·8	2·0	2·7	0·5	4·6	3·5	7·1	8·9	0·9
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	+ 0·367	+ 1·072
	2nd	Yeast fractions equivalent to 60 g. dried yeast daily for 10 days.	R.B.C.	..	1·875	..	..	..	..	2·060	..	..	..	..	2·265	..	..
			Ret.	..	0·9	0·4	1·1	0·9	0·7	2·0	0·8	2·7	5·0	0·1	1·1	..	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	+ 0·390	..	..
	3rd	Neo-Hepatex, 4 c.cm. alternate days for 3 doses.	R.B.C.	..	2·265	..	..	..	..	..	3·210	..	..	..	..	..	..
			Ret.	..	1·1	0·9	0·6	—	—	—	—	..	..	..	..	..	..
			Rise or fall.	..	..	..	..	..	..	..	+ 0·945	..	..	..	..	..	..
TMA 93 ♂	1st	Anahæmin, 4 c.cm. daily for 5 days.	R.B.C.	..	0·895	..	..	..	..	0·810	..	..	..	1·382	..	1·842 (14)	2·243 (18)
			Ret.	..	0·1	0·6	0·5	< 0·1	4·8	**18·6**	11·0	13·8	8·1	10·3	8·2	0·8	—
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	+ 0·487	..	+ 0·947	+ 1·348
NMA Monkey 7 ♂	1st	Anahæmin, 1 c.cm. daily for 10 days.	R.B.C.	5·925 (−46)	4·730	..	..	..	..	..	4·055	..	..	..	..	3·970 (13)	..
			Ret.	0·8	—	0·5	0·4	0·6	0·8	0·8	0·8	0·2	0·2	0·1	0·8	1·0	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	— 0·760	..
	1st	Campolon, 4 c.cm. daily for 5 days.	R.B.C.	..	3·970	..	..	4·260	..	..	..	..	..	..	4·975	5·595 (16)	..
			Ret.	..	0·9	0·6	1·0	0·5	**5·7**	4·9	3·3	2·6	0·4	1·1	1·9	0·3	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	+ 1·005	+ 1·625	..
NMA Monkey 45 ♀	1st	Anahæmin, 2 c.cm. daily for 10 days.	R.B.C.	3·580 (−16)	2·765	..	..	..	..	2·205	..	..	2·576	..	..	2·510 (12)	..
			Ret.	1·1	1·2	1·6	1·3	3·6	0·9	3·9	3·1	2·3	1·3	1·7	0·2	1·2	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	— 0·189	..	..	— 0·255	..
	1st	Campolon, 4 c.cm. daily for 10 days.	R.B.C.	..	2·510	..	..	2·677	..	..	..	2·760	..	..	..	3·570 (11)	..
			Ret.	..	1·2	1·4	1·1	3·2	3·9	6·7	9·0	7·5	9·4	**14·6**	3·4	5·3	..
			Rise or fall.	..	..	..	..	..	..	..	..	..	..	..	..	+ 1·060	..

* R.B.C. = red blood corpuscles per c.mm. † Ret. = reticulocytes per cent. ‡ All treatment starts on day 0.
§ PA = pernicious anæmia. TMA = tropical macrocytic anæmia. NMA = nutritional macrocytic anæmia.
‖ Rise or fall in red blood-cell count in millions calculated from day 0 of any period.
¶ Figures in parentheses indicate days before (−) or after beginning of treatment.

cent. on the fifth day and a rise in the red cell count of over 100 thousand per day. The clinical improvement was very striking. In the next 7 cases shown in the Table there was no response at all to anahæmin, though the doses were very high. These patients were all suffering from tropical macrocytic anæmia with the exception of the one sprue patient. All responded later to some cruder preparation, though the percentage of reticulocytes seldom reached the levels seen in correspondingly severe cases of pernicious anæmia similarly treated.

These results were clear-cut: there was no reticulocyte crisis, no clinical improvement, and no appreciable rise in the red cell count in any of these cases after treatment with anahæmin and in 5 the count fell during the 10-day test period. The eighth patient (Case 122) died of heart failure on the tenth day: on the fifth day only was there a rise in the reticulocyte count, the significance of which is doubtful as it may have been a terminal blood crisis. The last 2 patients require further note.

Case 25 showed some response to the enormous dose of 2 c.cm. of anahæmin daily for ten days but the improvement was delayed to the eleventh day, when the red cell count had risen from 0·803 to 1·170 million, an average daily increase of 0·033 million, a very poor response when compared with that of the pernicious anæmia case after a much smaller dose of anahæmin. Further, the reticulocytosis was slight and even after twenty-five days the count had only risen to 2·265 million in spite of additional treatment with a yeast extract, whereas when the treatment was changed to 4 c.cm. *Neo-Hepatex* (Evans Sons Lescher and Webb) every other day for three doses, there was an immediate rise in the count, the average daily increase being now 0·1575 million instead of the 0·058 million of the previous period.

Case 93 had a submaximal reticulocyte response and an average rise of 0·079 million a day over a period of eighteen days. This case is of some interest, as though by the hæmatocrit method it was a macrocytic anæmia, the Price-Jones curve did not show a macrocytic change. The initial rise of 0·487 million in nine days was poor though the final increase was fair: this latter may have been related to the fact that a urinary infection had been successfully treated.

The 2 monkeys suffering from nutritional macrocytic anæmia also failed to respond to the enormous doses of 1 and 2 c.cm. anahæmin daily for ten days, though this batch of anahæmin had been tested clinically in 2 cases of pernicious anæmia and shown to be highly active. Monkey No. 7 improved rapidly with campolon, 4 c.cm. daily for five days, and showed an average regeneration of 0·1015 million a day; monkey No. 45, which was very ill, had a late reticulocyte response, but by the eleventh day the red cell count had risen by 1·060 million and the monkey was greatly improved clinically.

The liver extract *examen* was tested next, as this preparation had also been completely inactive in the monkey anæmia (Wills, Clutterbuck, and Evans 1937) and in one case of tropical sprue. It is impossible however to assess its value in tropical macrocytic anæmia on the cases tested as, by chance, most of the patients either went out of hospital on the fifth or sixth day of treatment, or else developed malaria or some other complicating disease. It is possible that this extract is more active than anahæmin in the treatment of the tropical condition, but the few results obtained were so disappointing, in comparison with those obtained in similar trials with pernicious anæmia patients, as to suggest that the factor active in the tropical anæmia is only present in very small amounts.

For example, a typical pernicious anæmia patient with an initial count of 1·775 million red cells, after a single dose of only 4 c.cm. of examen, had 22·4 per cent. reticulocytes on the fifth day of treatment and a rise of 0·535 million red cells in ten days. In comparison, a woman with uncomplicated tropical macrocytic anæmia and an initial count of 0·876 million received the large dose of 2 c.cm. of examen daily for eight days; her maximum reticulocyte count was 18·0 per cent. on the eighth day and on the tenth day her count was still 0·800 million and by the seventeenth day it had only risen to 1·116 million. At this point she received 4 c.cm. of campolon on alternate days (5 doses): on the fourth day the percentage of reticulocytes rose again to 18·0 and by the tenth day her red cell count had risen to 2·330 million, a rise of 0·124 million a day.

Another case, a man with an initial count of 1·307 million, who received the enormous dose of 20 c.cm. in eight days, responded with a maximum reticulocyte count of only 12·2 per cent., but his red cell count rose by 0·625 million in eleven days, a poor response to such a very large dose. His further progress could not be followed as he walked out of hospital on the tenth day, after a test-meal.

The fractions made from *campolon* by extraction with saturated ammonium sulphate (Wills, Clutterbuck, and Evans 1937) did not give clear-cut results. It had been shown previously that this method of fractionation failed to separate quantitatively the liver principle, as both the ammonium sulphate soluble and the insoluble fractions were active in the cure of pernicious anæmia, the small dose of 2 c.cm. of either extract, equivalent to 4 c.cm. of original campolon, producing good reticulocyte responses and a submaximal rise in the red cell count of approximately 0·06 million a day—an excellent improvement after such a small dose of campolon. With larger doses maximal responses were obtained with both preparations. It is clear therefore that the liver principle, even in such small doses as must be present in the ammonium sulphate soluble fraction from 4 c.cm. of campolon, is highly active in true pernicious anæmia. It is otherwise in the anæmic monkeys and in tropical macrocytic anæmia. The monkeys failed to respond to the insoluble fraction, which should contain the bulk of the anahæmin-like principle, but responded to the soluble fraction.

Case 2 of the tropical series, who was treated with the same batch of extracts as the monkeys, also failed entirely to respond to the insoluble fraction though she made an excellent response to the soluble fraction. There was a rather small reticulocyte rise of 16 per cent. on the fifth day but a rise of 1·625 million in the red cell count in eleven days.

Case 123 had 20 c.cm. of the insoluble fraction, the equivalent of 40 c.cm. of untreated campolon, but had a maximum reticulocyte rise of only 16·6 per cent. on the sixth day; the count rose from 1 million to 1·855 million on the eleventh day but remained at this level till the seventeenth day, when the treatment was changed to 4 c.cm. of campolon daily for five days. This dose of campolon was equivalent to half the original dose given as the insoluble fraction: there was an immediate clinical improvement and the count rose rapidly by 1·030 million in eleven days, which suggests that there had been a very considerable loss of potency in the insoluble fraction.

The results of the clinical trial of *other batches of extracts* (of which the protocols are available for inspection) might be taken to indicate that the insoluble extract was the more active of the two, but actually it was impossible to assess their relative potency in these cases, as Case 19 was acutely ill and also pregnant and Case 35 was syphilitic. But it is obvious that the active factor was present in both these fractions in sufficient quantities to induce a response, when given in large doses.

DISCUSSION

The clinical trials reported above have shown that tropical macrocytic anæmia when treated with highly

purified liver extracts behaves in a manner similar to the nutritional macrocytic anæmia of monkeys. The liver principle curative in pernicious anæmia, when purified, is inactive in both conditions. This finding, if confirmed, must modify both the theories of ætiology and the principles of treatment. Assuming that the hæmopoietic activity of such preparations as anahæmin is due to the liver principle, a deficiency in the body of this principle can no longer be accepted as the cause of either tropical macrocytic anæmia or of sprue. Tropical macrocytic anæmia, like the nutritional macrocytic anæmia of monkeys, appears to be due to a deficiency in the diet of some factor at present unidentified but other than Castle's extrinsic factor. In sprue, if the deficiency is of the same order, it probably results from a failure of absorption rather than from a deficient diet.

The work of Jacobson and Subbarow (1937) suggests that in the cure of pernicious anæmia more than one factor is concerned. They describe a primary factor, which alone is very slightly active, and at least three accessory factors necessary to induce a maximum hæmopoietic effect. One of these accessory factors is *l*-tyrosine. At first sight it would appear that this work offers an adequate explanation of our findings. A lack of one or more of the accessory factors—tyrosine is excluded by experiments on anæmic monkeys (unpublished)—would account for the inactivity of preparations containing the purified liver principle or for their very slight activity (Cases 25, 93, 94). The difficulty in accepting this explanation lies in the fact that maximal responses can be obtained in pernicious anæmia after treatment with relatively small doses of such extracts as anahæmin and examen, which would suggest that all Jacobson's factors must be present in these preparations, as the presence of his factors was worked out for cases of pernicious anæmia. However, the theory of an accessory factor (though not necessarily one of those described by Jacobson and his co-worker), whose absence inhibits the action of the liver principle, would offer a reasonable explanation of our findings and also of the fact that certain patients with true pernicious anæmia are refractory to treatment with anahæmin but respond well to cruder extracts. But the possibility of the tropical anæmia being a distinct entity, in which there is no lack or inhibition of the liver principle, must be borne in mind. We were not able under the conditions of our work to do pigment metabolism estimations, but it is a striking fact that there was no increase in plasma bilirubin; in fact in the original series of cases studied this was lower than normal, and there was likewise no increase in the excretion of urobilin, such as occurs in untreated cases of pernicious anæmia (Wills and Mehta 1930). These findings suggest, but no more, that the increased hæmolysis which is a fundamental part of pernicious anæmia is absent in tropical macrocytic anæmia, and this indicates that the two diseases have a fundamentally different pathological basis.

Work on the essential nature of this new hæmopoietic factor has been reported for cases of both tropical macrocytic anæmia and monkey anæmia (Wills 1934, and Wills, Clutterbuck, and Evans 1937). The fact that the autolysed yeast extract, marmite, as well as crude liver extracts, both by the oral and the parenteral routes, are curative suggested that the missing factor is part of the vitamin-B complex. Assuming that the human and monkey conditions are the same and that if one type fails to respond to a certain fraction the other will also fail, then vitamin B_1, B_4, lactoflavin, and nicotinic acid (unpublished work with monkeys) can be excluded as the curative principle. The yeast-fuller's earth filtrate factor of Edgar and Macrae (1937) has not yet been separated from this new hæmopoietic factor.

In conclusion it should be emphasised that at present all cases of tropical macrocytic anæmia, and those cases of sprue which show a macrocytic anæmia, should be treated with the cruder liver extracts and not with purified extracts alone. When expense is an urgent problem the parenteral injection of a few c.cm. of some preparation such as campolon, supplemented by the daily administration of 30 to 60 g. of marmite, will in most cases of tropical macrocytic anæmia induce a rapid remission; marmite alone will often be sufficient.

SUMMARY

1. Tropical macrocytic anæmia does not respond to the more highly purified liver extracts, which contain the liver principle curative in pernicious anæmia in relatively pure form.

2. This fact further differentiates this disease from pernicious anæmia and demonstrates the presence of a new hæmopoietic factor in crude liver and autolysed yeast extracts.

3. This factor is almost certainly identical with the one described in the production and cure of the nutritional macrocytic anæmia of monkeys; it is not vitamin B_1, B_4, lactoflavin, or nicotinic acid but has not yet been separated from the yeast-fuller's earth filtrate of Edgar and Macrae.

4. For the treatment of tropical macrocytic anæmia crude liver or autolysed yeast extracts should be used.

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ENLARGEMENT OF LEWIS HOSPITAL.—Dr. T. B. Macaulay has just laid the foundation-stone of the £24,000 extension to the Lewis Hospital, Stornoway, which will double the present accommodation. Each new ward will be provided with a sun-room, and provision is to be made for a resident physician in addition to the surgeon. Of the cost of the extension £14,000 is being provided by the Department of Health for Scotland and the remaining £10,000 is to be found by the people of Lewis and Harris. Of this nearly £2000 has already been raised by the work of the extension appeal committee.

MENINGO-ENCEPHALITIS AND ORCHITIS AS THE ONLY SYMPTOMS OF MUMPS

By Wilfred Harris, M.D. Camb., F.R.C.P. Lond.

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Hugh Bethell, M.R.C.S. Eng.

In view of the recent and the frequently recurring epidemics of mumps, which is one of the minor scourges of our public schools, as well as of the public in general, we think it important to stress the fact that the term epidemic parotitis is an insufficiently descriptive name for mumps, which may run its course without any sign of parotitis whatever.

Though numerous records can be found of cases of mumps associated with meningeal symptoms, and of the absence of parotitis, yet the fact is probably insufficiently known that parotitis is only a common complication and not the essential feature of the disease, which is far better described by the old-fashioned name of mumps than by the pseudo-scientific term of epidemic parotitis.

On April 21st last, one of us (W. H.) saw a well-grown schoolboy of 17½, sent to him by Dr. R. H. Allport of Wonersh, with symptoms of meningitis. The boy had been isolated in the sick-room at his public school with German measles, and discharged and sent home on April 2nd. Two cases of mumps had been admitted to a neighbouring room in the sanatorium before he left, but as far as he was aware he had had no contact with them. On the evening of April 19th, 17 days after leaving school, he had severe headache and was sent to bed, the pain in the head becoming more severe during the night. On the following day he was much worse, vomiting after medicine, and was very drowsy all day, with a temperature of 101°–102° F. He remembers nothing of this day. The following day he was better, but his legs collapsed when he tried to walk. The temperature remained 101° F. His doctor found some symptoms of meningitis, and suspecting that it might be of cerebro-spinal type, sent the boy up for treatment.

On admission to the private wing of St. Mary's Hospital on April 21st, his temperature was 101·2° F. and his pulse 100. He had no headache, and he seemed quite bright and able to tell everything about himself, except what happened on the previous day. Flexing the head gave rise to some pain at the back of the neck; Kernig's sign was present, and some carination of the abdomen. The deep and superficial reflexes were normal, and also the eye movements, pupils, and optic discs. Lumbar puncture showed a pressure of 170 mm., not much above normal. The cerebro-spinal fluid was clear with no clot, no tubercle bacilli or other organism. Its content of chlorides was 0·69 per cent. and of leucocytes 740 per c.mm., 55 per cent. being lymphocytes. Although these findings, both clinical and pathological, supported the diagnosis of some form of meningitis, they were taken to exclude cerebro-spinal meningitis due to the meningococcus, and also tuberculous meningitis. The boy continued to vomit on taking any food or medicine on April 21st and 22nd. On the day following admission, April 22nd, the temperature was 100° F. and the pulse-rate 80; there was still pain on flexing the neck, and right orchitis had developed, the testicle being swollen, hard, and painful. There was no trace of tenderness of the breasts or parotids, or any pain on eating or opening the mouth. Fomentations were applied to the testicle, which by April 24th was less painful and not so hard. The temperature continued to oscillate from 99° F. to 101·4° F. until April 28th, when it fell to normal, the pulse keeping steady at 72 after April 24th. The pain on flexion of the neck and Kernig's sign had disappeared by then and two days later all pain in the testicle had disappeared too; this still remained swollen, though much softer on palpation. The temperature rose to its highest point (101·6° F.) on the evening of April 26th, and the next morning the left testicle was much swollen and tender. It was painted with glycerin and belladonna, and fomentations were applied; the left orchitis cleared up more rapidly than on the right side, pain disappearing after five days. Lumbar puncture was repeated on April 28th, when the pressure was 180 mm. and the fluid clear with 18 cells per c.mm. At no time was there any sign of parotitis or mastitis. The boy's convalescence was uninterrupted and he was discharged after disinfection on May 12th.

That the case was one of mumps, as shown by the alternating orchitis, admits of no doubt, and the acute incidence of the disease, with cerebral symptoms of headache and delirium and vomiting, accompanied by signs of meningitis, provides evidence that the stress of the infection first struck the central nervous system as a meningo-encephalitis. It is to be hoped that testicular atrophy may not follow the orchitis, as sometimes occurs after the orchitis of mumps.

That neither parotitis nor mastitis was present at any time during the course of the disease is interesting. Without the development of orchitis the diagnosis of mumps would undoubtedly have been missed.

One of us (H. B.) many years ago had a somewhat similar experience in his practice.

An adult aged 27 had a headache of sudden onset, temperature 101°–103·2° F. After the first day the temperature rose to 104·4° F. The pulse remained under 100; he was drowsy with slight delirium, and very constipated with general abdominal discomfort. Headache continued with stiffness of the neck and back; reflexes were normal. On the 5th day a swelling of right testicle appeared followed by enlargement of the left on the following day. Right testicle became very painful, swollen, and hard, more so than the left. Relief was obtained immediately on the application of leeches. Temperature began to fall on the 7th day after the onset. The headache and delirium disappeared as soon as the signs of orchitis became manifest. At no time was there any parotitis. The patient during convalescence suffered from giddiness when walking about slowly and he was unable to ride a cycle with comfort for six weeks. His wife contracted mumps from him, the infection running a normal mild course.

Since this note was written an excellent annotation has appeared on the same subject (*Lancet*, July 2nd, 1938, p. 32), in which lymphocytosis in the cerebro-spinal fluid of a small proportion of contacts with mumps is shown to appear on the 15th day, and the fluid was proved to be virulent. Dopter's suggestion that the virus of mumps is essentially neurotropic and that parotitis is only one of the possible metastases is certainly borne out by our cases. Additional evidence of the neurotropic character of the virus is the occurrence of neuritis following mumps. One of us (W. H.) five years ago saw a young man of 26 who after being ill for 10 days with parotitis and orchitis, 2 days later developed pain over the left shoulder and back accompanied by paralysis of the serratus magnus due to neuritis of the long thoracic nerve.

SOME BIOLOGICAL PROPERTIES OF DIETHYLSTILBŒSTROL

By S. J. Folley, M.Sc., Ph.D. Manch.

and

Helen M. Scott Watson, B.A. Camb.

(*From the National Institute for Research in Dairying, University of Reading*)

Recently Dodds, Lawson, and Noble (1938) have reported on various physiological properties of the synthetic œstrogen, 4′ : 4′-dihydroxy-α : β-diethylstilbene (diethylstilbœstrol) which was described by Dodds, Golberg, Lawson, and Robinson (1938). They found that this substance has a similar action to œstrone on the uteri of immature rats and rabbits and ovariectomised rats, on the vagina and the mating reaction of the immature rat, on the guinea-pig teat, and on the feathers of capons.

In view of the probability that diethylstilbœstrol will find important applications in clinical medicine and also in veterinary practice and animal husbandry, it is important to compare its physiological effects with those of œstrone in every possible respect. Diethylstilbœstrol was therefore tested for the three biological properties dealt with below, which are characteristic of œstrogens belonging to the œstrane series.

INHIBITION OF RESPONSE OF PIGEON CROP-GLAND TO PROLACTIN

Folley and White (1937) showed that the enlargement of the pigeon crop-glands due to administration of prolactin could be partially inhibited by simultaneous treatment with œstradiol monobenzoate. This effect has since been studied quantitatively by Folley (unpublished work), using œstrone.

TABLE SHOWING INHIBITION OF THE PIGEON CROP-GLAND RESPONSE TO PROLACTIN BY DIETHYLSTILBŒSTROL AND ŒSTRONE RESPECTIVELY

Experimental group received injections of—	Mean weight (Wc) of crop-glands of control birds.	Mean weight (W_E) of crop-glands of experimental birds.	Per cent. inhibition $\frac{(Wc-W_E)\times 100}{(Wc-Wu^*)}$
	g./100 g. bird.		
Diethylstilbœstrol ..	0·88	0·63	46
Œstrone ..	0·93	0·74	32

* Mean weight (Wu) of unstimulated crop-glands/100 g. bird = 0·34 g.

Two groups of 20 pigeons were used to study the action of diethylstilbœstrol on the crop-gland response, each bird receiving six daily subcutaneous injections of 1 ml. of an aqueous solution containing 1·5 mg. of a preparation of prolactin. Immediately after each prolactin injection, every bird belonging to one group was given a subcutaneous injection of 200 μg. diethylstilbœstrol in 1 ml. sesame oil, while each bird in the other (control) group received similar injections of sesame oil. In other respects the experimental procedure was similar to that previously described (Folley and White 1937). The percentage inhibition $\frac{(Wc-W_E)\times 100}{(Wc-Wu)}$ was calculated from the mean weights of the crop-glands of the experimental birds (W_E), of the control birds (Wc), and of a group of 20 birds which has received six daily injections of 1 ml. sesame oil but no prolactin (Wu). The results of this and a similar, though not simultaneous, experiment in which each experimental bird received 200 μg. œstrone daily are given in the Table. It will be seen that diethylstilbœstrol partially inhibiss the crop-gland response and that under these conditions it appears to be somewhat more active in this respect than œstrone.

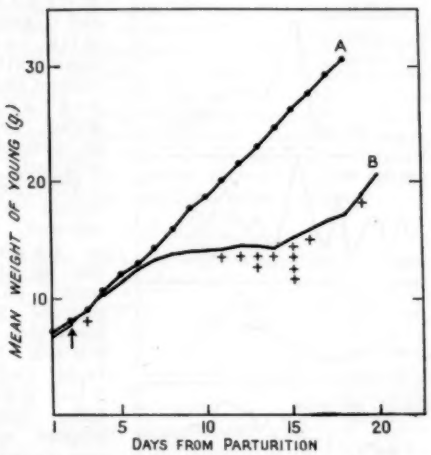

FIG. 1.—Inhibition of lactation in the rat by diethylstilbœstrol, injected at the point indicated by the arrow.
A. Average growth-curve for combined young of three rats given daily injections of 3 mg. diethylstilbœstrol in 0·5 ml. sesame oil, beginning on the second day of lactation. Number of pups at beginning of experiment, 13 males and 10 females. + signifies the death of one member of the litters of rats receiving diethylstilbœstrol.
B. Average growth-curve for combined young of two rats given daily injections of 0·5 ml. sesame oil beginning on the second day of lactation. Number of pups at beginning of experiment, 8 males and 8 females.

INHIBITION OF LACTATION IN THE RAT

That administration to lactating animals of natural œstrogens inhibits lactation is well known. Folley and Kon (1937), who give citations of previous work, found that lactation was markedly inhibited in rats which were given daily injections of 1 mg. œstradiol monobenzoate.

Three rats were given daily injections of 3 mg. diethylstilbœstrol, dissolved in 0·5 ml. sesame oil, from the second day of lactation until weaning or until all the young had died. Two controls received similar injections of sesame oil. Litters larger than 8 were reduced to that number immediately after birth. The average growth curves of the litters of both groups are given in Fig. 1, from which it is clear that lactation was inhibited in the rats receiving diethylstilbœstrol. This result is of interest in view of the clinical use of œstrogens for inhibiting lactation when for any reason it is desirable to do so (see, e.g., Ramos and Colombo 1938).

EFFECT ON THE COMPOSITION OF COW'S MILK

Folley (1936) found that administration of suitable doses of œstrone or œstradiol monobenzoate to cows in declining lactation causes certain characteristic changes in milk composition. The milk phosphatase (phosphomonoesterase A_1, see Folley and Kay 1936) content undergoes a substantial but temporary increase, while the non-fatty solids content and also the fat content are both raised for a considerable period.

Approximately 1 g. of crystalline diethylstilbœstrol was implanted subcutaneously into a dairy shorthorn cow in advanced lactation, which weighed approximately 500 kg. In Fig. 2 are plotted the daily milk yield, percentages of fat (Gerber), non-fatty solids (determined by evaporation) and lactose (Blackwood 1934) in combined morning and evening milk, and phosphatase content (King and Armstrong 1934) in morning milk only.

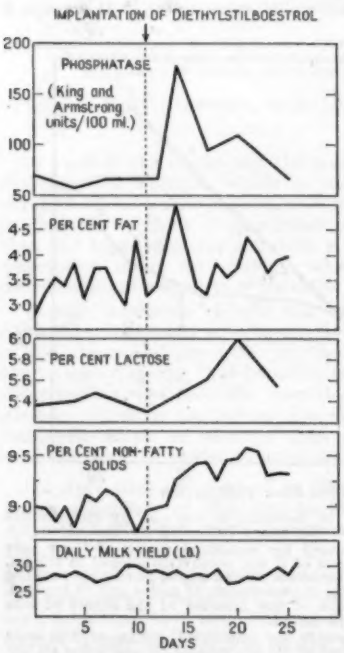

FIG. 2.—Effect of implantation of one gramme of crystalline diethylstilbœstrol on the yield and composition of cow's milk.

The treatment was followed by a sharp rise in the milk phosphatase followed by an equally rapid fall. The non-fatty solids content was significantly increased, the effect in this case being prolonged. Part of the rise in the milk non-fatty solids was evidently due to an increase in lactose, which suggests that diethylstilbœstrol does not cause the mammary gland to produce a secretion of colostral type, as was concluded by de Fremery (1938) to be the case in goats injected with œstradiol monobenzoate. In this respect also, the action of diethylstilbœstrol resembles that of natural œstrogens, since Folley (1936), on the basis of nitrogen partition determinations, concluded that colostrum is not secreted after administration of œstradiol monobenzoate to lactating cows.

Fig. 2 gives some indications that the treatment was also followed by a rise in milk fat, though the effect is somewhat masked by relatively large day-to-day fluctuations. It is interesting to note that the milk yield was practically unaffected by the treatment.

These preliminary results indicate a possible use for diethylstilbœstrol for improving the chemical quality of milk in cows which are secreting milk containing less than the legal minimum (8·5 per cent.) of non-fatty solids.

In conclusion it is of interest to note that while the above experiments indicate that, in all respects studied, diethylstilbœstrol has an action comparable to that of natural œstrogens on the *functioning* mammary gland, the preliminary experiment of Dodds, Lawson, and Noble (1938) indicated that this substance is less effective than œstrone in causing *growth* of the guinea-pig mammary gland.

SUMMARY

Diethylstilbœstrol has been found (1) partially to inhibit the response of the pigeon crop-gland to prolactin, (2) to inhibit lactation in the rat, and (3) to produce a temporary increase in the phosphatase content of cow's milk accompanied by more prolonged increases in both fat and non-fatty solids content. The latter effect was in part due to an increase in lactose content, which suggests that the treatment does not induce a change from normal milk to a colostral type of secretion. In all these respects the action of diethylstilbœstrol qualitatively resembles that of natural œstrogens.

We are indebted to Dr. S. K. Kon for providing facilities for working with rats, to Dr. F. G. Young for the gift of the prolactin, and to Prof. E. C. Dodds for the gift of part of the diethylstilbœstrol used in this work.

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CHRONIC MENINGOCOCCAL SEPTICÆMIA TREATED WITH 2-(*p*-AMINOBENZENESULPHONAMIDO) PYRIDINE

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WELL over 100 cases of chronic meningococcal septicæmia have now been recorded on the Continent. In America there have been far fewer accounts though Carbonell and Campbell (1938) and Appelbaum (1937) have produced notable reviews of the condition.

In England, so far as we know, no case has been published since 1936 when Stewart-Wallace described 3 which were seen in two years at the London Hospital. The condition can hardly be as rare as these figures suggest and, as the clinical picture is characteristic, more cases should be diagnosed.

CLINICAL FEATURES

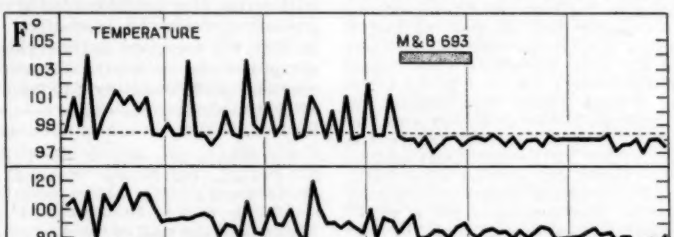
Occurring chiefly in young adults, the illness starts suddenly (less often insidiously) with headaches, chills, fever, and joint pains. The rash appears during the first week; typically it is rose-red and papular (rarely petechial, hæmorrhagic, or purpuric), scattered over the lower and upper limbs and, less commonly, on the face and trunk. The nodules come out in crops, roughly coinciding with the peaks of temperature, and begin to fade after 36–48 hours, leaving some brownish discoloration. The temperature, 99°–104° F., is intermittent and protracted and often accompanied by chills simulating those of malaria. The pulse-rate is in most cases slower than the temperature warrants. Arthralgia and myalgia are common and often acute rheumatism is wrongly diagnosed. The patient feels extraordinarily well considering the long-continued fever. The spleen is only rarely enlarged. Polymorphonuclear leuco-

cytosis of 10–20,000 is the rule and exceptionally there is a secondary anæmia.

The diagnosis is finally settled by blood culture but the illness is otherwise so characteristic that it should be suspected on clinical grounds alone, especially since blood culture is mostly negative in the first three weeks (Appelbaum 1937), and the meningococcus is notoriously difficult to cultivate. Many authors advise enriched media and incubation up to seven days before sending a negative report.

Rolleston (1919) states that chronic meningococcal septicæmia may (*a*) last for weeks without meningitic symptoms; (*b*) follow meningitis; (*c*) present transient meningitic symptoms: or (*d*) end in meningitis. The average duration of the fever is about twelve weeks, but it may last as long as a year. Left alone, the septicæmia tends to localise in the meninges or in the endocardium, but some cases recover spontaneously (Dock 1924). Thus in Carbonell and Campbell's review, 14 cases out of 33 developed meningitis, most of them late in the disease. According to Stewart-Wallace, about a quarter of the patients die, mostly from meningitis or endocarditis. Chronic meningococcal septicæmia, however, does not make the prognosis of terminal meningitis any worse.

Differential diagnosis.—Rheumatic fever, subacute bacterial endocarditis, influenza, erythema nodosum, erythema multiforme, typhoid, typhus, malaria, miliary tuberculosis, gonococcal sepsis, secondary syphilis, and undulant fever have all been considered in published cases.



Temperature chart showing course of illness from day of admission.

TREATMENT

Acute controversy has arisen over the question of the results of serum therapy, whether poly- or monovalent. The vast majority of recorded cases have had serum administered, often in enormous doses—e.g., a total of 600–1000 c.cs. French observers, however, are mostly sceptical of its value, and while some American writers are lavish in its praise, others are frankly disappointed. Even where serum has been most effective, the fall of temperature has been only gradual, taking at least 6–7 days to become normal. Failure has been variously attributed to inactive sera, inadequate dosage, to sera not containing antibodies for the particular infecting organism, or to a focus keeping up the blood-stream infection (Marlow 1929). Appelbaum has the impression that serum is valueless in the later stages of the disease.

Following the work of Proom (1937) it was to be expected that sulphanilamide would be used in this condition but there are so far only two published reports of its use. Schwentker, Gelman, and Long (1937) employed it in one case of meningococcæmia without meningitis, but this was included in a series of cases of cerebro-spinal meningitis and clinical details are meagre. They concluded that the effect of sulphanilamide was comparable to the effect produced by specific antiserum. On the other hand, in the two cases treated by Zendel and Greenberg (1937) the results were spectacular. In the first, massive doses of serum failed but sulphanilamide in large doses (40 c.cm. of Prontosil and 8·45 g. of sulphanilamide) greatly improved the clinical condition of the patient, brought the temperature down to normal in forty-eight hours, and rendered the blood sterile. In the second case no serum was used, but 100 c.cm. of prontosil and 5·66 g. of sulphanilamide produced the same result after sixty hours.

In the case here reported, neither serum nor sulphanilamide was administered, but since Whitby (1938) claimed that in animals 2-(*p*-aminobenzenesulphonamido) pyridine (hereafter referred to as M. & B. 693) is as effective as sulphanilamide against the meningococcus, it was decided to test his statement in man by using the former drug. A case such as this is better suited to demonstrate its antimeningococcal value, if any, than would be one of cerebro-spinal meningitis in view of the three clear-cut criteria—pyrexial chills, rash, and blood culture.

CASE RECORD

A man aged 20, who worked as a polisher, was admitted to St. Leonard's Hospital on June 2nd, 1938. He had had otorrhœa as a child but his general health had been good. He had been in bed for five weeks with "acute rheumatism." His illness started suddenly with a shivering attack, severe headache, malaise, and vague aches flitting from joint to joint; he had no difficulty in moving his joints. Shivering attacks occurred every other day, and after a week or two a few red spots appeared on his legs and arms. He felt well the whole time. He had no symptoms suggesting sinusitis or meningitis and no sore-throat.

On admission general condition good apart from mild pallor. Throat injected. Tongue coated. Some dental caries. Heart: reduplicated mitral first sound. Lungs clear. Abdomen normal. Spleen not palpable. No meningitic or other abnormal signs in the central nervous system. Fundi normal. Drums normal. A few rose-red raised tender nodules about 1 cm. across on both forearms and legs with two confluent nodules on the dorsum of the left foot. The nodules faded on pressure and were unaccompanied by itching. Many fading discoloured patches on both shins. Temperature 98·6° F., pulse-rate 104, respiration 22. The urine showed transient glycosuria, but the blood-sugar was normal. Throat swab: normal flora. Blood count: red cells 4,610,000, hæmoglobin 82 per cent., colour-index 0·89, white cells 15,800 (polymorphs 76 per cent., lymphocytes 22 per cent., eosinophils 1 per cent., monocytes 1 per cent.). Electrocardiogram normal.

Progress.—Fresh nodules appeared in crops while the others were fading, but towards the end of the first week there was a gradual improvement, no new nodules being seen for 3 days. The chief symptom was severe joint pains during this period. The diagnosis made was erythema nodosum with a severe febrile reaction, now subsiding. The Mantoux test 1 : 1000 was weakly positive; radiography of the chest was normal. On the 13th day after admission however, his temperature rose to 103·5° F. and this coincided with a fresh crop of nodules. A nodule 2 cm. in diameter appeared on the extensor surface

of the left forearm, two smaller ones on the right forearm and wrist, and a tiny one on each knee. Throat slightly injected. No physical signs elsewhere. No cardiac murmurs at any time. Next day another nodule appeared with a rise of temperature. Blood sedimentation-rate 51 per cent. in 1 hour (100 mm. tube).

It would be superfluous to recount the succession of nodules and the repeated pyrexial attacks (see Chart). In general, however, a crop appeared at about the peak of each daily rise of temperature and usually was immediately preceded by a chilly feeling not amounting to a rigor. One large nodule 2·5 cm. in diameter appeared in an unusual situation—over the right scapula. On June 20th, 19 days after his admission, the first blood culture was performed and Type 1 meningococci isolated after incubating 4 days in 0·2 per cent. glucose-broth. This was repeated on the 24th, and was again positive although only one Gram-negative diplococcus was isolated which failed to grow further on culture. Lumbar puncture on the 25th produced clear cerebro-spinal fluid not under pressure and yielding normal laboratory findings. The same day M. & B. 693 was started—1 g. at 3, 2 g. at 6, and 1 g. at 9 P.M.—all sulphur-containing foods and aperients being omitted. From the first dose there was no further rise of temperature (see Chart). The following day the patient had a reaction. He vomited five times and felt ill, but nevertheless 1 g. of the drug was given three times a day for the next three days, and 0·5 g. t.d.s. for another two days. It was finally discontinued on June 30th. There was no further reaction and the patient felt very well. Nodules present before the drug was given faded within forty-eight hours and no fresh ones appeared. Blood cultures on June 27th, 29th, July 1st, 6th, and 11th were all negative, although in each case incubation was continued for a week. Blood sedimentation-rate was 6 per cent. in one hour on July 4th. Nasopharyngeal swab gave a mixed flora but no meningococci. Radiography of the accessory nasal sinuses showed an opaque left antrum, but some thin pus obtained by proof puncture contained no meningococci. Blood count on July 4th: red cells 4,160,000, Hb. 84 per cent., white cells 7100 (polymorphs 50 per cent., lymphocytes 47 per cent.). Administration of M. & B. 693 was controlled by frequent white-cell counts but no adverse effect was noted. Before the drug was started the white cells were 6600, and afterwards they varied between 6300 and 11,500. The patient is ambulant, afebrile, symptomless, and has been discharged. The disease lasted in all about 8 weeks.

DISCUSSION

The case here described is typical of chronic meningococcal septicæmia, the outstanding features being (1) pyrexial chills occurring almost daily, (2) crops of nodules resembling those of erythema nodosum, (3) arthralgia, and (4) the crucial blood culture yielding the meningococcus. It will be noted that the pulse-rate was mostly below 100. The spleen was never enlarged and there was a moderate leucocytosis.

The focus of infection is often a mystery but the left antrum may here have been the source, in spite of a negative bacteriological finding after M. & B. 693 had been used. Embleton (1920) believes the sinuses are often infected in meningococcal cases. The nodules are presumably embolic (Rolleston 1919), and the accompanying sudden pyrexial chill and positive blood culture support this view. This feature also lends emphasis to the dramatic cessation of physical signs on the administration of M. & B. 693. Blood cultures were negative on all subsequent occasions—a fact which acquires significance when taken in conjunction with the sudden and complete cessation of daily pyrexial attacks, meningococcal emboli, and arthralgia. In view of the conflicting results of serum therapy, the alarming reactions it may cause, and the delay in bringing the temperature back to normal in even the most successful cases, M. & B. 693 certainly seems to have justified its use in this case. The dose given at the outset may have been too high, inasmuch as the patient vomited for one day, but experience is insufficient as yet to estimate the optimum dosage.

Comparing the effect of this drug with that of sulphanilamide in the two cases described by Zendel and Greenberg (1937), one is struck by the following differences: (1) M. & B. 693 acted at once, sulphanilamide only after an interval of 48–60 hours; (2) the dose of M. & B. 693 required was considerably less; and (3) vomiting occurred after M. & B. 693, whereas no reaction is reported after sulphanilamide. The results of treating cerebro-spinal meningitis with this new drug will be of the utmost interest.

SUMMARY

Chronic meningococcal septicæmia is characterised by recurrent pyrexial chills, crops of cutaneous nodules, arthralgia, and positive blood culture. The fever usually lasts several weeks. Treatment with serum may produce a fall in temperature in about a week or may be ineffective. In a typical case M. & B. 693 was given in the eighth week of illness and symptoms immediately disappeared. A transitory reaction with vomiting followed twenty-four hours after the first dose. This case encourages trial of M. & B. 693 in cerebro-spinal meningitis.

My thanks are due to Sir Frederick Menzies and to Dr. A. D. Morris, medical superintendent of St. Leonard's Hospital, for permission to publish and treat this case; to Miss E. F. Collins, Dr. J. M. Alston, and the staff of the Archway group laboratories (L.C.C.) for carrying out the investigations involved; and to Messrs. May and Baker for generous supplies of the drug used.

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STOMATITIS OF VITAMIN-B_2 DEFICIENCY TREATED WITH NICOTINIC ACID

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IT is nearly 25 years since Funk in England and Suzuki in Japan originally suggested that nicotinic acid was in some way related to vitamin B. This was a pregnant hypothesis which now seems to have been justified. In the last few years, the vitamin-B_2 complex has been found to consist of three components, one of which is the pellagra-preventing factor. It is now recognised that nicotinic acid is one of these components and that this substance is either the actual pellagra-preventing factor or its precursor.

Already favourable clinical results have been reported in pellagrins treated with nicotinic acid; thus Spies (1938) has published a series of 15 cases which showed rapid improvement on this treatment. All the cases so far reported have been typical of true pellagra; but we are convinced that a vitamin-B_2 deficiency often exists where most of the cardinal signs and symptoms of true pellagra are either obscured or absent.

The complete deficiency—pellagra—varies in its appearance and manifestations in different races and in different parts of the world. For instance, in the absence of strong sunlight, as in northern and temperate countries, the skin lesions do not become apparent, but the pellagrous tendency exists all the same. It follows that many minor conditions not previously regarded as pellagrous become dovetailed into the B_2-deficiency complex. They are characterised by an inflammation of the digestive tract with stomatitis and chronic diarrhœa. A small rather pointed angry red tongue with eczematous excoriations of the angles of the mouth, and a leucoplakic condition (perlêche) of the lower lip, may be taken as pathognomonic of the pre-pellagrous state.

One of us (P. H. M-B.) originally drew attention to this clinical picture during his work in Ceylon in 1912 and 1913. He was struck by the complete denudation of the lingual epithelium, with destruction of the papillæ and an associated angular stomatitis, which was to be encountered in a high proportion of the native prisoners who had been fed on a salted-fish diet completely devoid of fresh vegetables. The relation of this *sore tongue disease* to pellagra was then considered to be probable (Bahr 1915).

Since then the same condition has been described by Nicholls (1933) in Ceylon, by Wright (1928) in Sierra Leone, and by Fitzgerald Moore (1934) in Nigeria. In Malaya, Landor and Pallister (1935) described in detail this same symptom-complex which accompanies a vitamin-B_2 deficiency. In their cases stomatitis was an early and prominent symptom. In the first stages there was swelling and inflammation of the papillæ round the tip and margin of the tongue. The white fur was then lost and the final picture was of a small red tongue left quite smooth by denudation of epithelium. The corners of the mouth were affected more or less equally with the tongue. Symptoms such as paræsthesia of the legs, dimness of vision, and perineal eczema subsequently developed. Recently Stannus (1936) has made a masterly summary of all the symptoms which go to make up latent pellagra.

The purpose of this note is to draw attention to the benefit which may attend the administration of nicotinic acid in states which can be described as pre-pellagrous or as *pellagra sine pellagra*. An example is here described, and we submit that there must be many similar cases to be met with in general practice in this country.

CASE RECORD

A married woman, aged 62, who had been resident in South Africa from 1927 to 1929 was admitted to the Hospital for Tropical Diseases on June 12th, 1938. For five years she had suffered from morning diarrhœa. The bowels were open 4–6 times daily, and the stools were frothy, bright yellow, and very offensive. Soon after the onset of the diarrhœa the tongue became very painful, sore cracks appeared at the angles of the mouth, and there was increased salivation. About 18 months after the onset of the diarrhœa the patient complained of tingling sensations and numbness down the outer side of one leg; this symptom recurred in successive winters. Medical advice was sought on many occasions, but no permanent benefit was ever obtained either for the diarrhœa or for the stomatitis. Twice she was admitted to the local hospital and treated for gastric ulcer. Subsequently a diagnosis of sprue was substituted (although the patient had never lived where sprue is endemic) and she was treated with a non-protein diet.

When she was seen in June, 1938, the diarrhœa was severe and her mouth was extremely painful. The tongue was raw and denuded of epithelium with loss of all the lingual papillæ; she said that it felt several times its normal size. The saliva was acid in reaction. There were painful cracks at the angles of the mouth, and a well-marked grey line or perlêche on the lower lip.

Apart from psoriasis no skin lesion was found; there was no hyperkeratosis, and no history of abnormal sunburning. The cardiovascular, respiratory, and renal systems were normal, and except that the deep reflexes were exaggerated, nothing of consequence was found in the central nervous system. There was considerable distension of the abdomen.

The dried fæces contained 5 per cent. of fat, which was adequately split. The blood count showed a mild microcytic anæmia with a slight relative lymphocytosis. The blood-calcium was normal; the blood-cholesterol was 90 mg. per 100 c.cm. A fractional test-meal showed a considerable hyperchlorhydria with a second rise after histamine injection.

She was put on a full diet with an alkaline mixture and given 150 mg. of nicotinic acid (B. W. & Co.) daily. The diarrhœa ceased immediately and on the second day of treatment her tongue was slightly furred when she woke—the first time furring had been seen for five years. Within 48 hours the cracks at the angles of her mouth healed and the perlêche disappeared. At the end of ten days' treatment the patient was discharged. Growth of both filiform and fungiform lingual papillæ was then well advanced, and the feeling of malaise and depression, which had been present for five years, had entirely disappeared. Three weeks after the beginning of treatment the lingual papillæ were entirely normal and the patient had gained 5 lb. in weight. It is not an exaggeration to state that she was converted from a haggard into a healthy woman.

Intolerance to nicotinic acid has been previously described. In this case symptoms of intolerance were noticed after 150 mg. had been given daily for ten days. The dose was then reduced to 50 mg. daily, but manifestations of intolerance were noted again a fortnight later, so that this drug was discontinued as the patient appeared to be perfectly well. As she is now taking a full diet and absorption is not in any way diminished by intestinal hurry, there seems to be no reason why her symptoms should recur.

Regarding the toxic effects of the drug, the patient complained of stinging pain commencing at the angles of the jaw and passing upwards behind the ears. This was followed by faintness and flushing of the face. An itching urticarial rash appeared on the chest, arms, and front of thighs. No treatment was given and within half an hour all symptoms and signs of drug intolerance had disappeared.

American workers have shown that nicotinic acid does not affect either the "geographical tongue" or the glossitis of secondary or tertiary syphilis. At the Hospital for Tropical Diseases no improvement in the condition of the tongue has been seen in the characteristic stomatitis of sprue cases which have been tentatively treated with full doses of nicotinic acid.

SUMMARY

Nicotinic acid, one of the three components of the vitamin-B_2 complex, produces rapid improvement in true pellagra.

In temperate climates the skin lesions of pellagra do not appear and deficiency of the pellagra-preventing factor shows itself by stomatitis, a characteristic desquamation of the tongue, and chronic diarrhœa.

A woman of 62 had suffered from these symptoms for five years and recovered rapidly with 150 mg. of nicotinic acid daily and a full diet.

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PARALYSIS OF THE EXTERNAL PTERYGOID MUSCLE ARISING FROM INJURY TO THE FIFTH CRANIAL NERVE

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DURING the past twelve months I have seen three cases of paralysis of the external pterygoid muscle associated with loss of, or altered sensation in, the area supplied by the middle division of the fifth nerve. I have not been able to find any previous record of such an association. An interesting feature of the cases is that they were all due to the same type of injury—i.e., a blow on the same side of the face as that of the paralysis. This injury was accompanied by concussion causing loss of consciousness for times varying from a few hours to a few days. In two of the patients no sign of fracture of the bones of the face or head was demonstrable by radiography. In each case the symptoms were transient though in one they have not yet completely disappeared. Clinical details in the early stages were unfortunately meagre as the signs were not noticed until at least three weeks after the accident.

CASE 1.—A painter aged 24 was injured on Dec. 20th, 1936, in a motor-car collision. His chief injuries were to the "right side of the head" and top of the scalp. He did not know for how long he was unconscious, but thought it was possibly a few hours. I first saw him on Feb. 2nd, 1937, when he was complaining of persistent headache and noises in the right ear and of sharp pain in the right cheek and upper lip and numbness of the right side of the face. He said that for the past week he had been unable to read for more than 15–20 minutes without watering of the eye. He also had the headache and giddiness usual after concussion.

There was a soundly healed scar on top of the head, with no sign of any underlying bony injury and a small scar over the right eyebrow. No sign of ocular nerve paralysis was found. The sight of the right eye was not quite so good as that of the left but he could read ordinary newspaper print without difficulty. There was loss of sensation on the right side of the face, over the distribution of the middle division of the fifth nerve—i.e., over an area, including the right cheek and right half of the upper lip and right side of the nose extending back towards the ear. There were no signs of fracture of the malar bone or either maxilla or mandible and no antral hæmorrhage was revealed by transillumination. Movements of the jaw were painless but the chin deviated towards the right on opening the mouth. There was no deafness nor any sign of any intra-aural trauma. No bony injury was seen in the radiogram and a report from his doctor on April 18th said that all paralysis of the external pterygoid had disappeared.

CASE 2.—An insurance agent, aged 30, was injured on Sept. 17th, 1936, while riding a pedal bicycle which came into collision with a car. He was unconscious and remembered nothing for nine days after the accident and had to be detained in hospital until Oct. 10th. During this time there was some bleeding from the nose and a "watery discharge" from the left ear. A radiogram showed a fracture of the base of the skull. There was numbness and coldness of the left cheek, which persisted for six weeks after the accident, and also numbness of the legs, which persisted for about four weeks.

When I first saw the patient on March 2nd, 1937, there were no visible scars of the face or head, but there was numbness over the left eye corresponding to the position of the supraorbital nerve but only extending for about an inch up the forehead. He said that the skin had been cut over the eyebrow, but there was no visible scar. There was no pain or tenderness on pressure over the head or face, and no sign of gross ocular muscle paralysis, but there was double vision in the peripheral field. On opening the mouth the chin deviated to the left side. There was no deafness. On April 8th, 1938, hypersensitiveness of the left cheek to cold, peripheral double vision, and very slight deviation of the jaw were still present.

CASE 3.—A girl of 19 met with an accident on Jan. 4th, 1937, and was admitted to the Weir Hospital the same day. She was semiconscious and showed signs of cerebral irritation and photophobia. There was a large hæmatoma of the right frontal region and bleeding from the left nostril. A hæmatoma of the left eye extended down over the left malar bone and maxilla and there were abrasions of the left side of the face. Radiography on Jan. 6th showed no sign of bony injury. No abnormality of the movements of the jaw was noticed until Jan. 28th, when she mentioned that she had had a feeling of numbness and pins and needles over the left cheek. On that date I confirmed the fact that there was altered sensation over the distribution of the middle division of the fifth nerve including the left upper lip and side of the nose. On opening the jaw the chin deviated to the left. There was no sign of muscular weakness of the jaw or face other than that of the external pterygoid and no loss of sensation of the buccal or palatal mucosa. Three days later she had a transient conjunctival anæsthesia which lasted for only two days. On Feb. 2nd she was discharged from the hospital and all signs of paralysis had disappeared and sensation was normal.

COMMENTS

All three patients showed paralysis of the external pterygoid with loss of, or altered sensation in, the area supplied by the second division of the fifth nerve. In Case 3 there were no signs or symptoms suggesting fracture of the skull. In Case 1 the only clinical signs of fracture were bleeding from the nose and a watery discharge from the ear, with no radiographic evidence of fracture, while in Case 2 a fracture of the base was demonstrated by X ray examination.

The explanation of the association of these two signs is difficult. A peripheral lesion seems impossible as the sensory disturbance is clearly that of the whole second division and not of a single peripheral branch. The loss of power of the external pterygoid muscle might conceivably be due to local trauma causing hæmorrhage into the muscle, but the muscle is deeply placed and protected by the zygoma; nor was there any pain in the muscle in any of the cases. The only likely central site where injury might cause such an associa-

tion of signs is near the foramen ovale and foramen rotundum; through the foramen ovale passes the third division of the fifth nerve, of which the nerve to the external pterygoid is a part; and through the foramen rotundum passes the middle division of the fifth nerve. An obvious criticism of this explanation is that there was no sensory disturbance of the third division of the fifth. It is an argument in favour of the lesion being at this site that in one case a fractured base was demonstrable radiographically and in another there were clinical signs of such an injury; while the proximity of the nerves involved suggests the possibility of temporary damage to them.

It appears that a blow on the malar region of sufficient violence to cause severe concussion is necessary to bring about this injury; for since I saw these cases I have not come across another although I have examined very many cases of head injury. None of these however had suffered the exact type of blow met with in these cases.

The failure to observe these associated symptoms in the past is probably due to their being masked by the more obvious symptoms of concussion and their transient nature. It is likely that the symptoms are not uncommon after an injury to the side of the face and indicate a lesion at the base of the skull, resulting in fracture or hæmorrhage or both, in the neighbourhood of the foramen ovale.

Clinical and Laboratory Notes

UNDULANT FEVER TREATED WITH PRONTOSIL

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Last November Bethoux, Gourdon, and Rochedix described the successful treatment of a patient suffering from undulant fever, probably caused by the melitensis type, with compounds of the sulphanilamide group. The evidence that the successful outcome was attributable to the remedy is not altogether convincing, for the patient's temperature had already fallen to normal before the treatment was begun. Moreover considering that the fever had lasted for four months it is not improbable that the natural termination of the disease was just being reached. In February of this year Richardson reported two cases of infection by *Brucella abortus* treated with Prontosil which offer stronger proof that recovery was attributable to the administration of the drug; though here again, in one of the cases, there appears to have been an interval of five months between the onset of the disease and the institution of treatment. Francis at the same time reported two other cases of apparent cure, together with the results of some experiments in vitro which suggest that *Br. abortus* is considerably more susceptible to the action of sulphanilamide in vitro than is *Streptococcus pyogenes* under the same conditions. Lloyd (1938) and Mathews (1938) have also cited single examples of apparent benefit from the sulphanilamide group of drugs in the treatment of undulant fever.

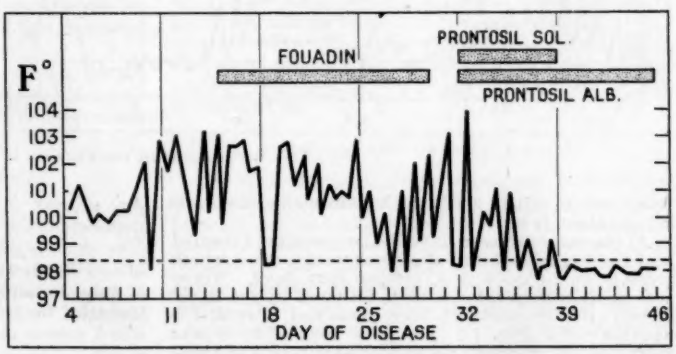
The case here recorded was seen by me three days after the onset of the illness and treatment with prontosil was instituted four weeks later, after Fouadin had been tried without apparent advantage.

The patient, a man of 36, was seen by me on Feb. 11th, 1938. He had been feeling "off colour" for about a month and had had some pyrexia for three days. His illness had started with generalised aching and shivering; there was sweating and complete loss of appetite, and the stools had been pale grey for three days.

On admission into a nursing-home on Feb. 11th he looked pale and ill. The temperature was 100·6° F., the pulse-rate 80, and the respirations 22 per minute. The tongue was furred and nothing abnormal could be felt in the abdomen. The spleen was not palpable. No abnormal physical signs could be detected in any system. A leucocyte count on Feb. 14th showed 5200 white cells per c.mm. (polymorphs 50 per cent., eosinophils 2, basophils 1, lymphocytes 32, and hyalines 15). Serum withdrawn on Feb. 16th contained no agglutinins for typhoid or paratyphoid A and B, but agglutinated *Br. abortus* up to a dilution of 1 in 800. Examined on Feb. 12th the stools were acid, containing a little starch but no other abnormal residue; there were a few flakes of mucus but no blood or pus. Cultures gave a growth of *Bacillus coli communis*, enterococci, and numerous colonies of a non-lactose-fermenter which proved to be *B. asiaticus*.

Progress and treatment.—On Feb. 26th the spleen became definitely palpable. From Feb. 22nd to March 8th fouadin was given by intramuscular injection. Injections were given on alternate days starting with 1·5 c.cm. and increasing the dose by 1 c.cm. till 5 c.cm. were being given; thereafter 5 c.cm. were given every other day, 32 c.cm. being administered in all. During this treatment the patient's symptoms persisted, his general condition deteriorated somewhat, and the temperature showed no signs of falling. On March 9th the serum still showed agglutinins to *Br. abortus* up to a dilution of 1 in 800.

On March 11th, the 29th day of the illness, prontosil therapy was started. Two tablets of prontosil album (sulphanilamide), each of 0·5 g., were given three times a day and 10 c.cm. of prontosil soluble intramuscularly each day. After a week the prontosil soluble was discontinued and the prontosil album, 3·0 g. a day by mouth, was given alone for a further week. After the first injection of prontosil the temperature rose to 104° F., but it then subsided and was normal by the seventh day of treatment (see Chart). The general condition rapidly improved and the pains, lassitude, headache, and anorexia disappeared. On March 23rd the serum showed agglutinins to *Br. abortus* up to a dilution of 1 in 400. The patient was sent home on March 24th;



Temperature chart showing apparent response to prontosil.

the temperature taken morning and evening for the next six weeks showed no rise above the normal, and he returned to his work feeling quite well. I saw him in June and he told me that he had had no relapse.

It seems justifiable in this case to attribute the patient's recovery to his treatment with prontosil.

I am greatly indebted to Dr. F. A. Knott for carrying out the pathological investigations in this case.

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UNDULANT FEVER IN A SANATORIUM

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During the past six months, in a study of causes of pyrexia in our patients other than that due to the tubercle bacillus, two cases of undulant fever were found. These are sufficiently rare to merit a short description.

Case 1.—A man of 29 developed pulmonary tuberculosis in March, 1937. A successful artificial pneumothorax was induced in April. He remained at rest in bed for four months, and in September went convalescent to a North Wales seaside resort where he frequented a milk-bar.

In the third week of September he came under observation complaining of anorexia, nausea, and vomiting for three days, with a remittent temperature up to 101° F. There were no localising symptoms and the pneumothorax was satisfactory. The urine was found to contain a little albumin and a few pus cells; and his symptoms were at first attributed to pyelitis. But alkalis failed to produce any but temporary improvement and a further detailed investigation showed no abnormality of the urinary tract. The pus had disappeared and the urine was sterile. A blood count showed a leucopenia (4800 white blood-cells) with an absolute lymphocytosis (58 per cent.). The blood-serum gave a negative Widal test but agglutinated the *Brucella abortus* in a dilution of 1 in 2500 which confirmed a diagnosis of undulant fever.

At the end of sixteen days the temperature subsided and there was an interval of four weeks, after which pyrexia again developed, lasting four days. There was another interval of a week followed by ten days' fever; the temperature then remained normal for another week (Fig. 1). The next bout of fever was milder and it gradually subsided over a period of three weeks. There were no further relapses. An effusion developed in the pneumothorax during the third period of pyrexia and was gradually absorbed.

Case 2.—A few weeks later a man aged 23 came under observation. Five weeks previously, after malaise for two days, he had had pyrexia with a slight rigor. He was in bed "off and on" during these five weeks with fever, cough, and expectoration, and was admitted for observation at the end of this time. He complained of weakness, cough, sputum, and loss of weight. There were no localising signs; the sputum showed no tubercle bacilli, and a radiogram of the lungs no infiltration. Two days after admission he developed fever, with anorexia and nausea especially in the morning. The white blood count was normal (8000 white blood-cells) and there was an absolute lymphocytosis (69 per cent.). His blood-serum agglutinated *Br. abortus* in dilutions up to 1 in 2500 which was held to justify the diagnosis. He continued to have bouts of fever of 2–5 days' duration for six weeks (Fig. 2) after which the temperature finally subsided. He, too, was accustomed to drink raw milk.

We were now on the look-out for the proverbial third case and we were not altogether disappointed. The second patient went home during convalescence and called to see a friend who used to feed at the same canteen and who was now ill in bed suffering from a fever of uncertain origin. Our patient told of his own diagnosis. His friend's blood was examined and found to agglutinate *Br. abortus* in high dilution; and after a somewhat similar course his fever too subsided.

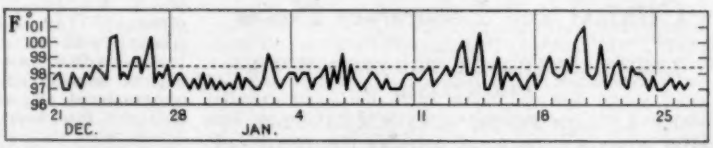

FIG. 2.—Course of fever in Case 2.

The features of the two cases under observation were bouts of remittent fever lasting from 3 days to 3 weeks and occurring over a period of three months. The temperature was highest in the afternoon and there was often a slight rigor. Anorexia, nausea, and occasionally vomiting were present during the period of pyrexia. There were no symptoms in the intervals except weakness but the patients lost weight. Both cases showed an absolute lymphocytosis, one a normal white cell count, the other a leucopenia. The serum of both agglutinated suspensions of *Br. abortus* in high dilutions (1 in 2500). Mild depression was noted during the pyrexial periods. The sedimentation-rate was raised during the illness and returned rapidly to normal at its termination.

Sulphanilamide in doses of 0·5 g. three times daily was tried for four days in Case 1, but its only apparent effect was to increase the nausea.

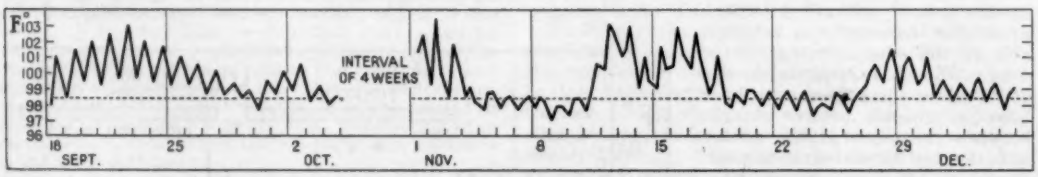

FIG. 1.—Temperature chart in Case 1.

(*Continued at foot of opposite page*)

BRITISH MEDICAL ASSOCIATION

SECTION OF DISEASES OF CHILDREN

AT the first session of this section Dr. LINDSAY DEY (North Sydney, Australia), vice-president, took the chair when a discussion was held on the

Modern Decline of Breast-feeding

Dr. J. C. SPENCE (Newcastle-upon-Tyne) said that prosperity and social comfort had not encouraged breast-feeding. Most women of fashion of the eighteenth century had hired a wet-nurse, the mother-substitute of that time. Now it was the cow and there was no mother in the country who could not obtain it if she wished. The curtailment of the reproductive cycle by failure to lactate was surely both a matter of clinical importance and a social experiment of scientific interest. The infant mortality in this country remained twice that in many countries and in some industrial towns it was three times that of similar towns in Australia. That meant that of the 40,000 infant deaths a year 20,000 were preventable. By contrast there could not be more than about 8000 people in this country with pernicious anæmia, and yet the scientific and clinical interest involved in the treatment of these old people was out of all proportion to that devoted to the prevention of those 20,000 deaths. It might be thought that the encouragement of breast-feeding was well recognised as one of the methods of combating the infant mortality but there were many who disagreed.

Dr. Spence thought that, apart from supplementing in the first few days when the milk yield might be small, 20–30 per cent. of babies were artificially fed from birth in many if not in most of our big towns and that not more than a third were fully breast-fed to six months. Bottle-feeding was a habit which rapidly spread and a further decline was likely in breast-feeding. It was possible that hospital physicians, seeing so much of sick infants, exaggerated the dangers of artificial feeding; but it was beyond all question that breast-fed infants enjoyed a greater freedom and power to recover from disease—the figures relating to pyloric stenosis and those of Grulee and Sanford in Chicago showed that. There might also be remote effects which have not been recognised.

Apart from the observation that repeated lactation in malnourished women might produce anæmia, little was known of the effect of lactation or its curtailment on women. It might be suspected that curtailment might engender endocrine disorders. The effect of lactation on the mother's character, temperament, and outlook deserved equal consideration with the physical effects but it had received little study.

The breast tissue and nipples developed during pregnancy in response to ovarian hormones. Immediately after parturition the ovarian hormones, which inhibited lactation, subsided and prolactin, from the pituitary, established lactation; later it was maintained by this hormone secreted under nervous reflex influences. Two of these were the frequent emptying and the emotional state of the mother. Fear, doubt, anxiety, and lack of interest inhibited lactation. Emotional disturbances involving the father were, in the speaker's experience, the greatest inhibitors. The mother's behaviour fell into three stages after parturition: after a period of profound rest for one or two days came the establishment of lactation, when the mother should be allowed to fondle her child as often as she wished and without any fixed rules about three- and four-hourly intervals. The mother then needed to be segregated, preferably in her own room; it was a period of peculiar jealousy reactions. The third stage was when the mother took on the care of the infant.

Lactation failed because mothers could not, would not, or knew not how to suckle. In rural districts 95 per cent. of the mothers breast-fed; it was likely, therefore, that only a small proportion were incapable for physical reasons. The blame for those who would not fell partly on those who advised them. The chief cause of failure, however, was mismanagement. The attitude of the maternity nurse was of supreme importance. The essence of the fault in most hospitals and nursing-homes was too great an attempt to mechanise breast-feeding. They had institutional rules about times of feeding, the amount, the weighing and test-weighing. If the feeding was at first unsuccessful the anxiety aroused made lactation harder. The lying-in room was becoming too much a combination of a sick-room and a flower-decked reception room; there should be no test-weighing and no temperature-taking of the infant unless clinical observation indicated it; and there should be no bottle-feeding of a healthy baby for a week. Furthermore the mother should have her own room; if this could be afforded for the inmates of prisons it should be possible to afford it for the mothers of babies. But probably the most important cause of failure among those who wished to suckle was the temporary inhibition of lactation when the mother returned to her household duties. This could be overcome largely by allowing the mother to be out of bed a few days before returning home and by explaining the inhibition. Dr. Spence thought that the mother should cultivate an instinctive recognition of her baby's needs, that she should come to know when the baby was satisfied and that she should then choose the times of feeding most suitable to herself and her child. Only in difficulties should professional advice be sought. In conclusion the speaker attributed the decline in breast-feeding to indifference to its value and to mismanagement. The correction lay with those who advised the mother in the early stages. Big wards and crowded welfare centres did not provide the atmosphere which encouraged it.

PITUITARY AND OVARIAN ACTIVITY

Mr. S. J. FOLLEY, Ph.D. (National Institute for Research in Dairying, Reading), spoke of the endocrinology of lactation. He said that the œstrogenic hormones of the ovary had been shown to be responsible for the growth of the mammary duct system and in some species for the growth of the gland tissue also. The additional action of the corpus luteum hormone (progesterone) appeared to be necessary in some species—in monkeys and therefore probably in man too. The œstrogenic hormones

(*Continued from previous page*)

The incidence of undulant fever in man is not definitely known, but it is probably more prevalent than is generally supposed. In Denmark in 1929 Kristensen [1] found that 10 per cent. of 4000 cases of unexplained fever were due to *Br. abortus*. It should also be noted that 20 per cent. of cases of undulant fever do not show agglutinins in the blood.

[1] Kristensen, M., and Holm, P., *Zbl. Bakt.* 1929, **112**, 281.

probably promoted mammary growth by way of the pituitary; in 1928 Stricker and Grueter had observed that the developed mammary gland was brought into action by a positive stimulus from the anterior lobe of the pituitary. It was now believed that lactation was initiated and maintained by this hormone (prolactin) which also possessed the power of causing growth of the crop-glands in the pigeon. Hypophysectomy stopped lactation when established, and if performed in pregnancy made lactation impossible; but refined prolactin, together with the adrenotropic hormone, could reverse this. Thyroid hormone increased the amount and quality of milk secretion in cows but had the reverse effect in goats.

Prolactin was usually assayed by its crop-gland growth promotion but recently the relation of this property to clinical effect had been doubted. Dr. Folley and Dr. F. G. Young had studied the effect of single injections of anterior-pituitary extracts on cows in declining lactation and had found that the correlation of the powers to promote crop-gland growth and lactation was low, but lactogenic potency showed a good correlation with glycotropic (anti-insulin) activities. They had obtained evidence of more than one lactogenic factor. Folley's recent results had suggested that there were two crop-gland promoters, one only being inhibited by œstrone.[1] If it should transpire that only one possessed lactogenic properties the discrepancy between crop-gland promoting and lactogenic powers would be explained.[1]

Dr. AUDREY RUSSELL (London) discussed the relation of ovarian activity and menstruation to failure of milk secretion. She had found that of 440 women who had amenorrhœa for twenty-four weeks of lactation, 5·6 per cent. of the infants needed supplementary feeds or were weaned, while of the 310 who menstruated before the twelfth week of lactation 73 per cent. needed it. Lactation had been satisfactory in 27 per cent. of cases in spite of ovarian activity. Examination of suction curettings of the endometrium had been made by Miss Gladys Dodds at University College Hospital. So far 47 cases had been examined. In 6 women with lactation amenorrhœa and good lactation histories there was atrophy of the endometrium closely resembling that seen after castration, indicating complete absence of ovarian activity. In 31 cases (in 10 of which lactation had been unsatisfactory) hypertrophic changes were found corresponding to the follicular phase of the normal cycle; of these, 12 remained in this stage for six weeks without bleeding. In the remaining 10 cases lactation had been unsatisfactory and the endometrium of the luteal type, ovulation having presumably occurred.

Selye and his co-workers had shown that suckling alone could inhibit the gonadotropic function of the pituitary and could induce milk secretion in non-parous animals. The initial post-partum secretion was independent of the suckling stimulus, but Dr. Russell held that the failure to maintain and increase the secretion, which happened in more than half the nursing mothers, arose because the suckling stimulus was not sufficient to maintain lactogenic and inhibit the gonadotropic functions of the pituitary. The secretory reflex, called "the draft," which occurred when the baby was put to the breast was easily conditioned. Its loss was fairly constantly one of the first signs of a failing breast; when it failed, a fairly accurate forecast of the onset of bleeding could be made. Dr. Russell showed a method of giving milk by catheter beside the nipple so that the breast received extra stimulation.

[1] See review by Dr. Folley in last week's issue of THE LANCET (p. 389).

MANAGEMENT AND DIET

Dr. ETHEL CASSIE (Birmingham) said that the general opinion among health visitors and medical officers with whom she had discussed the matter was that breast-feeding was diminishing and that this was so because the mothers were over-anxious or because they were going out to work. They concluded that on the whole the diminution did not matter because artificial feeding was easy and safe. It was thought to present few disadvantages physiologically or psychologically, the children seeming even more confident, independent, and happy. Breast-feeding was, however, encouraged because it was safer with the careless mother. It seemed therefore that the advocacy of breast-feeding might not always be as whole-hearted as some would desire. The centres themselves were said to play their part in the diminishing breast-feeding. However much the doctor and visitor might urge breast-feeding the mother saw beautiful babies thriving on dried milk and put her child on the bottle, very often with excellent results. Dr. Cassie thought diet an important factor: recent authoritative statements showed that the nursing mother required a high protein value in her diet which the working-class mother did not obtain; she thought that was why breast-fed children were less well developed. She was convinced herself—perhaps without proof—that breast-feeding was best, but the mother's diet needed supervision and hence indirectly the quantity and quality of breast milk. She thought that the giving of free milk must encourage artificial feeding; it was not given in Birmingham. The child was often weaned at the gap between the departure of the midwife and the arrival of the health visitor.

Dr. C. K. HAMILTON (London) said it was difficult to estimate the extent to which breast-feeding was failing; the figures varied widely from clinic to clinic, probably depending on the management of the mothers. Breast-feeding required careful handling and probably was too often classed as a natural process, left to the mother's instinct, and given up when it failed. Instances where breast milk disagreed were very rare and chemical analysis was so unsatisfactory as to be no guide. In management the mother should not be allowed to reduce the number of feeds in an attempt to conserve her milk; she should be calmed, if need be by sedatives. Digestive upsets of the child by overfeeding should be avoided. The mother should be taught about breast-feeding at antenatal clinics and be able to obtain advice at any time especially when she first took over her household. Breast-feeding should be the subject of more teaching to medical students and health visitors.

The CHAIRMAN thought the omission of training in the feeding of infants from refresher courses would be a great weakness. Common sense in the nurse and confidence in the mother were most useful in promoting breast-feeding. As regards results he felt sure that the reduction in infant mortality in Sydney by two-thirds in the last 25 years had been due to stemming the tide of artificial feeding.

Dr. J. GREENWOOD WILSON (Cardiff) had examined 300 school-children whose medical histories were known from infancy and had found no significant difference in the health of those that had been breast-fed and those that had been artificially fed. He thought artificial feeding was easier to manage

well than breast-feeding. Unrest and pleasure-seeking were perhaps the strongest influence against breast-feeding at present.

Dr. P. DE FREMERY (Holland) described his experiments on goats which showed that in the female kid a few drops of milk could be obtained from the breast after prolactin injection but development of the gland tissue only occurred if œstrogenic hormone were given, too, for three weeks. Neither effect was obtainable in the male.

Dr. A. G. WATKINS (Cardiff) spoke of the scanty training of doctors in breast-feeding, the students often being discouraged from being in the wards at feeding time. Mothers should not think of child-bearing as a process lasting but nine months; they should add another nine for feeding; they should be instructed before the birth rather than when they had the anxieties of the child.

Dr. RUTH YOUNG (India) said that in her clinics the diet of the mothers was incredibly poor: as Hindus they were forbidden to eat meat, fish, or eggs; they were too poor to buy milk and they had little fruit. The infants usually gained steadily on the breast for the first seven or eight months, but remained stationary or lost after that, weighing perhaps 12–15 lb. at eighteen months or two years when they were commonly still breast-fed. If the mother's diet was so important how could the successful eight months be accounted for? Did the bad effects only operate after then?

Dr. ALAN MONCRIEFF (London) considered that Dr. Greenwood Wilson's figures comparing children leaving school were incomplete. The figures given by Dr. Spence showed that a higher proportion of bottle-fed children died; the corresponding proportion did not come up for their school-leaving examination because they were dead. He thought there was a danger of making too much fuss about nutrition. A poor diet during lactation might cause anæmia but the milk did not fail in quantity until the woman was about to drop; and even then the quality remained. He agreed on the contagious character of bottle-feeding; he expelled rebel mothers from the ward. He had noticed a type of middle-aged spinster nurse who put the child on a bottle to obtain greater control of the child in conscious or unconscious satisfaction of her mother love. In reply to Dr. Spence he said he thought weighing and figures essential; without them a green hunger stool was often diagnosed as over-feeding. The alternative to regular feeding was a return to the middle ages.

Dr. D. E. MASON (London) said that breast abscess was common in the East End of London, perhaps because the breasts were not emptied or the diet too rich. She thought insistence on giving both breasts four-hourly often caused overfeeding leading to fretfulness and weaning.

Dr. E. C. DAWSON (Derby) blamed grandmothers and neighbours for premature weaning.

Dr. F. M. B. ALLEN (Belfast), president of the section, thought students and nurses should be given a dogmatic line to follow in managing breast-feeding.

Dr. SPENCE suggested a reversion to tribal habits to keep the male from his partner for more than 14 days after childbirth. He was surprised that belief in overfeeding existed. Some even doubted the benefits of breast-feeding: possibly the cow-like life of women in a totalitarian State had something to commend it.

SECTION OF MEDICINE

AT a meeting of this section with the president, Dr. T. H. G. SHORE, in the chair, the subject was

Toxic and Infective Jaundice

In opening, Dr. C. E. LAKIN (London) said that he was proceeding on the assumption, now generally accepted, that the parenchymatous cells of the liver had nothing to do with the formation of bile pigment, that the pigment was derived from hæmoglobin liberated from effete red corpuscles, and that the transformation of hæmoglobin into pre-hepatic bilirubin was due to the activity of the reticulo-endothelial system.

Jaundice might arise in three different ways. The first was obstructive jaundice where there was damming up of bile in the excretory ducts with absorption into the blood stream of post-hepatic bilirubin, bile salts, and cholesterol. The second was hæmolytic jaundice, where excessive blood destruction led to the accumulation in the blood stream of such a large amount of pre-hepatic bilirubin that the excretory functions of the liver were overpowered. The third was the so-called toxic or hepatogenous jaundice, where the liver itself was damaged so that it became unable to work at its normal level. Damage of liver cells with resultant toxic jaundice could be caused by poisons such as phosphorus and arsenic, by microbic activity or protozoal or virus infections, by some autogenous toxin as in toxæmia of pregnancy, and possibly by anoxæmia in congestive heart failure. As regards symptoms in toxic jaundice, the patient was usually more ill than jaundiced; the stools might remain fairly normal in colour; fever was usual except in the more severe forms; the urine contained varying quantities of bile with urobilin and albumin; the blood-sugar fell in severe liver damage; and in spirochætal jaundice there might be an increase in blood-urea owing to coincident damage to the kidney.

Pathologically the essential lesion in toxic jaundice was damage to the parenchymatous cells of the liver with, in some instances, an associated cholangitis. With massive doses of toxin, acute necrosis of the cells resulted, as in acute toxic hepatitis or in acute yellow atrophy. With less virulent and smaller repeated doses of the injurious agent a gradual replacement fibrosis resulted, as in chronic hepatitis or cirrhosis of the liver. The post-mortem appearances in fatal cases showed great variation. In phosphorus poisoning the liver was usually greatly increased in size, doughy in consistency, and yellow in colour; whereas in acute yellow atrophy the liver, except in the most virulent type, was reduced to perhaps a third of its normal size with a wrinkled capsule.

Catarrhal jaundice presented the problem as to whether it was hepatic or obstructive. Till recent years it had been assumed, on certain post-mortem evidence, that obstruction arose from inflammatory swelling of the mucosa at the ampulla of Vater or from infection ascending the common bile-duct. It had now been suggested, after study of its epidemic form, that all cases of so-called catarrhal jaundice were in reality cases of primary liver damage—i.e., that damage to the liver cell was the fundamental lesion though it might vary as to severity and extent within wide limits. It was seldom that post-mortem findings helped to decide this difficulty, as catarrhal jaundice was rarely fatal, and such post-mortem results as had been reported gave conflicting evidence. Moreover, we had to realise that even severe damage to the liver could occur without giving rise to jaundice.

On the clinical side evidence was not wanting of the close association of catarrhal jaundice and acute necrosis of the liver. Sir William Willcox estimated that about 0·4 per cent. of cases of catarrhal jaundice ended in a condition resembling acute yellow atrophy or necrosis of the liver. This being so, must every case of catarrhal jaundice be regarded as a potential case of acute yellow atrophy? Sir Arthur Hurst met the difficulty by suggesting that there were really two forms: (1) catarrhal jaundice proper, in which blocking of the common bile-duct occurred secondary to an acute gastroduodenitis; (2) mild forms of subacute hepatic necrosis. In distinguishing between the two forms stress was laid on the mode of onset. In the obstructive form there were initial symptoms of an acute gastritis with malaise and raised temperature, but by the time the jaundice had fully developed the temperature fell and the patient felt well except for nausea and vomiting if he partook of fatty food. At this stage epigastric tenderness had disappeared, though the liver might be slightly enlarged and tender and the gall-bladder and spleen palpable. In the second type, mild subacute hepatic necrosis, Hurst stated that there were no pre-icteric symptoms, and that the onset of jaundice was accompanied by symptoms of general toxæmia and a raised temperature. There was no epigastric tenderness, though the liver might be tender and slightly enlarged, and the spleen was always palpable.

Personally Dr. Lakin had found a little difficulty in agreeing with the statement that no pre-icteric symptoms were found in most cases of this type. In his experience of epidemic catarrhal jaundice there had been fever four or five days before the jaundice appeared, with nausea, vomiting, and discomfort in the upper part of the abdomen. He was not convinced that the two forms of the disease did not exist, but he found it difficult, from a consideration of the mode of onset, to get much help in distinguishing between the two types. The van den Bergh reaction did not give much help, but perhaps more might be claimed for the newer form of the lævulose-tolerance test, though in only four out of eight cases of catarrhal jaundice investigated had an abnormal curve been found.

The other point which he would like to touch upon was the possibility of a progressive lesion of the liver, which as in nephritis might be latent over a period of years. It had been pointed out by Bloomfield that many people who had suffered from an attack of catarrhal jaundice showed evidence of impaired hepatic function in the form of a high bilirubin content. Certainly one came across cases of relapsing subacute hepatitis in which, after perhaps three or four attacks of jaundice spread over a couple of years, the final attack was attended by signs of portal congestion and ascites as in the terminal stage of multilobular cirrhosis. Finally, he would like to say what a real contribution to clinical medicine would be made by anyone who would place on record the details of even a few cases of catarrhal jaundice followed from its onset to its termination.

Dr. A. W. SPENCE (London), speaking for Prof. G. R. Cameron, said that toxic jaundice was produced by liver damage, and that classification was of little value as all the destructive agents produced similar effects. The time-table of events showed three stages in the pathology of severe liver damage: acute yellow atrophy, where large areas of the liver cells were destroyed and the patient died in a few days; subacute atrophy, where destruction was accompanied by liver cell regeneration, and the duration of the illness was one to eight months; and multiple nodular hyperplasia or cirrhosis, where the final injury in the case might not be due to the initial agent. In some instances primary carcinoma of the liver might follow after some years. There were a number of factors which influenced the action of hepato-toxic agents and there were also personal variations. One factor was the amount of poison reaching the liver. If this was a large amount it led to acute liver atrophy. Another factor was the interval between successive exposures. There were also personal idiosyncrasies for certain poisons, and diet no doubt played a part, as there was evidence that excess of carbohydrate in the diet protected against chloroform poisoning. Associated infection was apt to increase the hazard, and there was evidence to show that some poisons were more liable to affect young people. Pregnancy might be an adverse factor and might weigh the balance on the wrong side. Alcohol increased the susceptibility of the liver to certain poisons. The subject was still obscure and there was need for pathologists and clinicians to join and investigate it.

Major H. C. BROWN (London) gave a brief description of some of the more important factors in the epidemiology of Weil's disease as it occurs in the British Isles. He drew attention to the fact that it occurs essentially in the labouring classes and that, with the exception of fish workers and tripe dressers, women are very seldom attacked. Direct or indirect contact with rats appears to be necessary. In dealing with the diagnosis of the disease a differential blood count was shown to be of considerable assistance when it is a matter of diagnosing Weil's disease from a florid and sporadic case of epidemic catarrhal jaundice. In the usual diagnostic procedures, such as agglutination tests and the isolation of the leptospira, attention was paid to the necessity for neutralising the patient's urine before injecting it into animals. Obscure influenzal states in the labouring classes, in which association with rats can be traced, should always be looked upon with suspicion. Ambulatory cases of Weil's disease had been met with as well as instances in which there is conclusive evidence of an infection having taken place although the individual has never reported sick.

Dr. G. W. M. FINDLAY (London) spoke on epidemic catarrhal jaundice. This, he said, might be obstructive, but in its epidemic forms he considered that the lesion was primarily a hepatitis. He thought that until there was more conclusive evidence for obstruction the term epidemic catarrhal jaundice might be dropped, and "epidemic hepatitis" substituted. Some years ago it was thought that they might be dealing with a Weil's infection, but this had not been proved. In the last two years there was considerable evidence that it was a virus infection. This arose from the results of yellow fever inoculation, where it was found that in addition to the immediate reaction a percentage of those inoculated were developing symptoms of jaundice from two to seven months after inoculation. The symptoms were similar in all cases, with a prodromal period of malaise of three to fourteen days. In attempts to avoid this, inactivation of the serum was found to be useless, as was also the taking of serum from subjects with a 'clean bill of health. Last December the strain of the yellow fever virus was changed and since then no cases had occurred. Similar outbreaks of hepatitis had been recorded in horses following the use of horse serum for immunising purposes. It appeared that there might therefore be a virus in immune serum. There was a long incubation period in these cases of from sixteen months to two years.

Dr. E. R. CULLINAN (London) spoke on the clinical features of toxic jaundice. The condition was subacute rather than acute, and the syndrome more common than was realised. The outstanding feature was complete absence of any ætiological factor, and post mortem nothing was found to account for the liver necrosis. Histologically the lesions were diffuse and not focal. The main clinical features were attacks of jaundice accompanied or preceded by vague ill health or gastric disturbance. There might be a little fever at the onset, but there was absence of fever when the jaundice was well developed. There was no loss of weight and the mouth was clean and moist. There might be occasional nose-bleeding and in the older cases hæmatemesis or melæna. The disease was painless, colic not being a feature. The jaundice varied in intensity and fluctuated during an attack, from day to day or week to week. Jaundice might last from two weeks to years and in one particular case it had lasted ten years. The liver was usually enlarged and sometimes its outline was irregular. The spleen was palpable in one-third of the patients. Ascites occurred in a long attack or at the end of a series of attacks, and only in the last few days might symptoms of severe liver failure appear as a terminal event. The urine was never found to contain leucine or tyrosine and the colour of the stools varied. The van den Bergh reaction was of no value in distinguishing toxic from infective jaundice. In duodenal intubation thin bile was obtained throughout, and in a radiogram the gall-bladder shadow did not show or was very faint, owing to an inability of the liver to secrete bile. This last point was important to remember as accurate diagnosis might save the patient from useless and possibly fatal laparotomy. The treatment consisted in giving glucose in sufficient dosage. Calcium sodium lactate orally or calcium gluconate intravenously was helpful, as was the exhibition of alkalis.

DISCUSSION

Sir ARTHUR HURST (Windsor) was fully convinced that one could distinguish catarrhal jaundice from other forms. He found the lævulose test essential in making a diagnosis but it should be done at a comparatively early stage, as in the later stages of all obstructive jaundice there was bound to be some liver impairment. He would like to emphasise the extreme danger of operation on infective or toxic jaundice. He agreed that the van den Bergh reaction was quite valueless in differential diagnosis. It was important also to remember a different class of case—namely, where jaundice came as a complication of a more or less long infection and where the prognosis was good. He thought that in view of the danger of Atophan (cinchophen) producing a toxic jaundice, it should never be given without first doing a lævulose test.

Dr. DONALD HUNTER (London) questioned the similarity between the symptoms of catarrhal jaundice and Weil's disease. He thought that in Weil's disease the patient was severely ill, with hæmorrhage and fever, whereas catarrhal jaundice took a milder form. He asked if there was any evidence that the leptospira went through unabraded skin.

Dr. G. S. ASTON (Barnstaple) had found in his experience that the incubation period for so-called catarrhal jaundice was 21 days. The liver was often enlarged and there might or might not be fever.

Dr. BELL WALKER (South Africa) said that in epidemic jaundice in South Africa the disease was not apparently conveyed from individual to individual. Nearly all his cases occurred in children from 4 to 14 years, and boys preponderated. Fatal cases were quite common, especially in relapse. He often found a consequent impairment in health in those who had suffered from catarrhal jaundice. He quoted a case of catarrhal jaundice in a girl of 14 years who had succumbed to acute yellow atrophy with her first pregnancy some years later.

REPLIES

Major BROWN maintained that the differential diagnosis between epidemic catarrhal jaundice and Weil's disease was not easy, as one could get both diseases from a subclinical, right up to a very florid, condition. The two points which helped were the differential blood count and the intense muscular pains of Weil's disease. South Africa was said to be free from Weil's disease, but Dr. Bell Walker's description of the epidemic jaundice in his area made him wonder if Dr. Walker was not dealing with Weil's disease.

Dr. FINDLAY pointed out that some observers had found hepatitis without obstruction in post-mortem examination of catarrhal jaundice. He confirmed the long incubation period in infective hepatitis. The disease might occur in such a minor form that the incubation period would appear falsely short.

Dr. LAKIN said he was interested to find that other speakers confirmed his experience of the long incubation period in epidemic catarrhal jaundice. He had also been supported in the possibility of a progressive lesion of the liver. It would appear from evidence that one attack of jaundice could leave behind it an impaired liver, and that, after a latent period of some years, a precipitating cause such as pregnancy might prove too much for the previously impaired organ.

SECTION OF PHARMACOLOGY

BOTH sessions of this section were largely taken up with anæsthetics. Prof. A. J. CLARK (Edinburgh), from the chair, read a paper on certain aspects of the

History of Anæsthetics

The discovery of anæsthetics was, he said, the only pharmacological advance of any importance made in the nineteenth century which had reached mature development and could therefore suitably be treated from the historical aspect. It was the first occasion on which the synthetic products of the organic chemist were used to produce a therapeutic effect of major importance. He recounted the historical facts leading to the use of nitrous oxide, ether, and chloroform. In 1844 Horace Wells, an American dentist, produced surgical anæsthesia with nitrous oxide; in 1846 he repeated the phenomenon with ether and in 1847 Simpson introduced chloroform. In 1846 the only mention of anæsthesia in THE LANCET was a short note in the last number of the year on the use of ether; less than four months later (April 10th, 1847) the Editor referred to ether as "a remedy which had already produced such an unparalleled influence on the practice of surgery in this country" and stated that the number of operations had doubled. Throughout 1847 THE LANCET maintained a special column in each number describing "operations without pain." Many advances had been made since then but undoubtedly ether, nitrous oxide, and chloroform were together more important than all other known agents. After this remarkable advance there followed a long period of quiescence and it was only during the last 15 years that active search for new agents had recommenced.

The credit for the discovery of ether had been a matter of prolonged controversy, well summed up by Jacob Bigelow in a letter to Simpson (1870): "as far as we know he (Morton) is the only man, without whom anæsthetic inhalation might have remained unknown to the present day." Discoveries were seldom the sole work of a single individual; all research workers stood on the shoulders of their predecessors, and if current knowledge was adequate to suggest a possible advance to one person it was certain that the same idea had already occurred to many others. There was however a great difference between an original idea and a successful achievement. The main credit must always go to the person who possessed the energy and determination to demonstrate the possibility of progress along some new path. The search for a substitute for ether was conducted to a successful issue by Simpson, David Waldie, chemist to the Apothecaries Company in Liverpool, and Duncan. After the religious outcry had been overcome chloroform was widely used but deaths from its use soon began to be reported. Snow, in a masterly analysis of 50 deaths from chloroform, showed (1858) that in at least 40 death was due to cardiac syncope and not to overdosage acting on the brain and medulla. Numerous commissions, set up to inquire into deaths from chloroform, all ascribed the fatal results simply to overdosage, quite overlooking the importance of Snow's observation.

Looking to the future it was clear, said Prof. Clark, that after a technique had become efficient the chances of major advances were diminished; but the example of engineering showed that continuous small advances could be collected together until they constituted a major improvement. It would be generally agreed that further advance in the technique of anæsthesia was desirable. The fact that deaths under anæsthesia were increasing indicated that perfection had not been attained. A stage had been reached when further progress could only be made by coördinated work, similar to that created at Oxford, under the guidance of the Nuffield chair of anæsthetics, which would permit the accurate estimation of new methods adequately controlled by the laboratory worker and the clinician.

Dr. J. T. HUNTER (London) read a paper on

Anæsthesia in Thoracic Surgery

Its two major difficulties were, he said, manifest: the disease itself decreased the vital capacity of the patient, and there was the problem of sputum. Both could be partially overcome by adequate preparation of the patient, such as rest in bed, administration of fluids with glucose, postural drainage, or the production of artificial pneumothorax on the affected side. Premedication must be light—e.g., Omnopon gr. 1/3 with scopolamine gr. 1/150, followed by a rapidly acting basal anæsthetic. He had found sodium Pentothal suitable for the purpose. For lobectomy or thoracoplasty a spinal anæsthetic was excellent; that technique was introduced by Shields of Toronto who used procaine dissolved in the patient's own cerebro-spinal fluid. In 1936 Magill began to use the 1 in 1500 solution of Percaine according to the Howard Jones technique. In 1937 Rink and Harris modified that technique so that a unilateral anæsthesia was produced. The advantages of spinal analgesia were the absence of bleeding, the retention of the cough reflex, freedom from cyanosis, and undisturbed respiration. If general anæsthesia was required ether was excluded owing to the hypersecretion of mucus it produced. Chloroform was too dangerous to use alone but was a good adjuvant to gas-and-oxygen. The latter was non-toxic, non-irritating, and produced little after-effect; but it had to be remembered that alone it might easily decrease to dangerous limits the amount of oxygen in the blood of a patient whose vital capacity was already lowered by disease. Ethylene was out of place owing to its smell and the risk of explosion. Cyclopropane had certain advantages: (1) 80–85 per cent. of oxygen could be used in the anæsthetic mixture, (2) respiratory movements were slight, (3) the gas was quickly excreted, and (4) it was non-toxic and non-irritating.

Dr. Hunter then outlined the type of anæsthetic technique applicable to certain thoracic operations. For phrenic avulsion and rib resection local anæsthetic drugs were the most suitable. For apicolysis and extrapleural pneumothorax it was found that cyclopropane was more efficient than gas-and-oxygen. In most cases of thoracotomy and lobectomy spinal analgesia was more suitable than any form of general anæsthesia, especially if sputum was present. At the Brompton Hospital all bronchoscopy work was done under local anæsthesia using 20 per cent. cocaine after suitable premedication.

Anæsthesia in Cardiac Surgery

Dr. J. K. HASLER (London) said his experience of anæsthetics in cardiac surgery had been gained in the cardiac clinic of Lambeth Hospital under the direction of L. F. O'Shaughnessy. In the past, surgery of the heart had been concerned solely with operations for the removal of shrapnel, the repair of stab wounds, and attempts at removal of pulmonary emboli. Recently in diseases producing ischæmia of the heart operations had been undertaken to improve its blood-supply by grafts of fat and muscle. Every such patient would be classed as a bad risk, for he was middle-aged or elderly and, in the majority of cases, subject to anginal pain as a result of slight exertion, cold weather, or emotion. The routine procedure was to give sufficient basal anæsthetic to ensure that the patient was just asleep or very drowsy when brought to the theatre. Thus the evening before he had a sleeping draught of chloral hydrate and bromide. One hour before operation omnopon gr. 1/3 with scopolamine gr. 1/150 was given by mouth and half an hour before operation Nembutal gr. 1½ was given in the same way. If the patient was not asleep at the end of the half-hour the nembutal was repeated and the operation postponed. Induction was commenced with ethyl chloride followed by ether on an open mask. Anæsthesia was maintained with an ether-and-oxygen mixture supplied by a Tiegal-Henle machine to a closely fitting rubber face-piece. Positive pressure was attained by a device which forced the patient's expirations under water. The heart was exposed by the left transpleural approach; through a slit made in the diaphragm the omentum was stitched either to the left ventricle or to the pericardium covering the ventricle. When the chest was opened and the left lung collapsed the anæsthetic mixture was supplied under positive pressure, which was increased still further while the chest was being closed. After operation the patients were kept at rest for two to three months until the graft had well taken. From the anæsthetic point of view no anxiety at all arose during the operation and the speaker attributed this to the large amount of oxygen used in the anæsthetic mixture. One death was probably partly due to the anæsthetic, that of a man who died of pneumonia ten days after operation.

REVIEWS AND NOTICES OF BOOKS

Text-book of Nutrition

By J. A. NIXON, C.M.G., M.D., F.R.C.P., Emeritus Professor of Medicine in the University of Bristol; and DOREEN G. C. NIXON, M.B., B.S., M.R.C.S., L.R.C.P., Recognised Teacher of Hygiene in the University. London: Humphrey Milford, Oxford University Press. 1938. Pp. 219. 7*s.* 6*d.*

THE time is not ripe for dogmatic statement. Prof. and Mrs. Dixon quote with approval this characteristic saying of Michael Foster's and apply it to the many controversial topics which arise throughout their study of nutrition. The result is a useful little book which covers a large field in very small compass. The physiology of food digestion, absorption, and metabolism are fully discussed in the first three chapters, which are followed by a fourth on the vexed question of the assessment of the state of nutrition. In five and a half pages the authors set out the fundamentals of the position, indicating in what directions progress may be looked for. While they tacitly accept Prof. Lydia Roberts's conclusion that there is at present no practical method of judging the child's state of nutrition which has the sanction of scientific authority, yet they agree with her in not wishing to discontinue routine clinical examination although its shortcomings are patent. The chapter ends on the hopeful note that help will be found on lines similar to those laid down by Burnet and Aykroyd. Subsequent chapters are concerned with practical questions of food and diet. Separate sections are devoted to vitamins and minerals, to the choice of food, to tables of food values, and to the relation between diet and income. The rest of the book summarises our knowledge of diseases of nutrition and their cure, as well as the dietetic treatment appropriate to other disorders.

To do more than sketch the main features of a rapidly developing subject would be impracticable in a book of this size. Though too condensed to be fully adequate as a text-book, it supplies the need for a well-balanced general introduction to the modern conception of nutrition and dietetics. The omission of references (apart from the name of the investigator) for the statements made makes it less serviceable than it might have been for those who propose to study in further detail the points raised. In the tables, however, the authorities are cited. The details given of the composition of various foods as regards protein, fat, carbohydrate, and the different minerals will be particularly useful to those who have to plan special diets.

Essentials of Obstetrical and Gynecological Pathology

By MARION DOUGLASS, M.D., F.A.C.S., Assistant Professor of Gynecology, Western Reserve University, Cleveland; and ROBERT L. FAULKNER, M.D., Senior Clinical Instructor in Gynecology in the University. London: Henry Kimpton. 1938. Pp. 187. 21*s.*

GYNÆCOLOGICAL pathology like dermato-histology often suffers the ignominy of being squeezed into some corner of works on general pathology and undergraduates seldom learn much about it except during their training in clinical gynæcology. Drs. Douglass and Faulkner have sought to help them by this readable survey. The account of each section of the genital tract is prefaced by a description of the normal anatomy and histology and the endometrial cycle and changes in the organs during pregnancy are particularly well explained. The distinction between pseudo-malignant and premalignant conditions of the cervix is made clear and the various microscopical and macroscopical ways of grading cervical carcinomata are detailed. A complete classification of ovarian tumours is set out, but only the dozen or so commoner types are discussed. The various solid tumours derived from embryological rests are described and differentiated.

Our chief criticism of the book concerns the illustrations. Many are excellent, but some of the more important ones, such as those of the endometrium, are very poor. The book is printed on art paper, but the screen used is much coarser than is customary in the best British and Scandinavian half-tone reproductions. The fault probably lies in the quality of the actual photomicrographs. Throughout the book, however, British readers will have to interpret unfamiliar terms such, for example, as "female English bull" which is used for what we would call a bull-dog bitch.

Seasonal Periodicity of Malaria

and the Mechanism of the Epidemic Wave. By CLIFFORD ALLCHIN GILL, Col., I.M.S. retd., M.R.C.P. Lond., D.P.H., D.T.M. & H., late Hon. Surgeon to H.M. The King; late Chief Malarial Medical Officer, The Punjab. London: J. and A. Churchill. 1938. Pp. 136. 10*s.* 6*d.*

THIS book centres round relapse in causing seasonal and epidemic waves of tertian and subtertian malaria, and as a first step divides the world into malarial zones. In the temperate zone, with Holland as the type area, the mean temperature in the hottest month lies between 16° and 20° C., and only tertian malaria is found. It shows a slight autumn rise, due partly to relapse and partly to new infections, and a conspicuous spring wave due to delayed primary attacks which have been latent since autumn. In the subtropical zone, which has South Italy for its type area, the mean temperature in the hottest months lies between 20° and 25° C., and the geographical limit between it and the temperate zone is placed along the line where subtertian malaria appears. Here tertian malaria has its main wave in autumn as the result of fresh infections, while a small spring wave is caused by relapses with perhaps some latent first attacks to swell it; the general autumn rise in malaria is however partly caused by the subtertian parasite with the peak of its wave in September. North India is taken as the type area of the tropical zone; the mean temperature in the hottest months is 25° C. and the mean monthly humidity is less than 50 per cent. for at least one month in the year. The seasonal characters of the infection are in the main those of the subtropical zone, but the high autumn wave carries a morbidity and mortality unknown elsewhere, for at that time there is both high temperature and high humidity. The equatorial zone—with Ceylon for its type area—has a mean monthly temperature never less than 25° C. and a mean monthly humidity never less than 77 per cent. It is in fact not a geographical unit but a series of separate areas, most but not all within the geographical tropics. Here endemicity and epidemicity of malaria show themselves in waves normally of low

height, but in epidemic years both are equally and greatly heightened.

The book sets out the reasons which have convinced Colonel Gill of the importance of relapse in initiating certain seasonal and epidemic waves. These he outlined in a paper communicated to the Royal Society of Tropical Medicine and Hygiene some time ago (see *Lancet*, 1936, **1**, 322) and he has now elaborated them with much care. In his view the two factors—one determining the seasonal relapse and one controlling transmission—concerned in the mechanism of the seasonal relapse are sometimes dissociated. The spring wave in the temperate and subtropical zones he regards as an example of a seasonal wave due to the relapse. But his thesis is too complex to admit of summary and those interested in the theory should study this book. If his reasoning is accepted it follows that the essential problem now before malariologists is to find the real cause of seasonal relapse.

Hernia

Second edition. By LEIGH F. WATSON, M.D., Member of Attending Staff, California Lutheran Hospital, Los Angeles. London: Henry Kimpton. 1938. Pp. 591. 31*s.* 6*d.*

IT is remarkable that a book of some 600 pages devoted entirely to the rather limited subject of hernia is not tiring to read. This one is obviously the work of an expert and is well arranged. Dr. Watson, while not ignoring theoretical possibilities, gives a clear straightforward expression of opinion on any matter of controversial interest. His anatomical diagrams are excellent if occasionally redundant, and his operative details are well illustrated and described. Perhaps the most interesting fact about the book is that its author was led to prepare a second edition by his observation of the increasing use of the injection treatment. To this part of his subject he now devotes some 100 pages and he testifies in his preface to his conviction, based on experience, of the value of this treatment (for certain types of reducible hernia) and of its far-reaching economic importance to industry. This aspect of injection treatment is again emphasised in a brief medico-legal chapter at the end of the book. Apparently one of the American States now offers injection treatment to 90 per cent. of the men making claims on account of hernia attributed to industrial causes. The clear exposition here given of the technique and results of this method suggests that in this country it has not received enough attention.

Neurology

Second edition. By ROY R. GRINKER, M.D., Chairman, the Department of Neuropsychiatry of the Michael Reese Hospital, Chicago. London: Baillière, Tindall and Cox. 1937. Pp. 999. 38*s.*

THE author of a text-book of neurology has a difficult task deciding how his material is to be arranged and where the emphasis is to be placed. Dr. Grinker has chosen to cover as wide a field as possible within the limits of organic neurology. He devotes much space to embryology and the naked-eye anatomy of the nervous system, and though this helps to make the book complete in itself it necessarily limits the space available for clinical neurology, which is likely to be the main interest of most readers. The treatment of this subject, though mostly adequate, is sometimes rather bald and one looks in vain for those illuminating thumb-nail clinical sketches at which the older writers seemed to be more adept than their successors. Whether the neuroses should find a place in a text-book of clinical neurology is, perhaps, a moot point, but they are clearly important in differential diagnosis, and the lack of any mention of the symptomatology of hysteria in this book is a serious omission. Neurology is developing rapidly and all important recent advances seem to be recorded here.

A Guide to Veterinary Parasitology

For Veterinary Students and Practitioners. By T. SOUTHWELL, D.Sc., Ph.D., Walter Myers Lecturer in Parasitology, School of Tropical Medicine, University of Liverpool; and A. KIRSHNER, M.B., D.T.M., Assistant Lecturer in Parasitology at the School. London: H. K. Lewis and Co. 1937. Pp. 144. 7*s.* 6*d.*

UNTIL quite recently the English veterinarian was severely handicapped through lack of a modern guide to the important and ever-increasing subject of animal parasitology. In 1929 Baylis had, indeed, published a manual of helminthology, but this work, admirable as a zoological treatise, dealt almost exclusively with the morphology and classification of the adult internal parasites, omitting those essential data concerning their development, life-histories, and host reactions which should characterise a work described as "medical and veterinary." The year 1934 saw the almost simultaneous publication of two books which gave up-to-date presentations of the subject; unfortunately Mönnig's treatise excluded the parasitic protozoa and that of Cameron the insect parasites, so that it was necessary to possess both treatises to cover the subject completely. These works were designed for, and efficiently met, the needs of veterinary surgeons. When the Royal College of Veterinary Surgeons revised its syllabus for the M.R.C.V.S. diploma and included in the extended curriculum veterinary parasitology as a separate subject, a much briefer exposition was urgently required. This small and concise volume incorporates in condensed form the lectures which the senior author has given during the last twenty years to veterinary students in Liverpool, and presents the subject to the beginner in a simple, elementary, and practical manner. Lengthy descriptions of the morphology of the various parasites have been avoided, and only points of diagnostic importance are stressed. Prophylactic measures are discussed at greater length than the pathological effects of infection. The opening chapter gives brief instructions on the proper use of the microscope and the simpler methods of staining blood films. Succeeding chapters deal with pathogenic protozoa, cestoda, trematoda, and nematoda. Separate chapters are devoted to the methods for the preservation and examination of fæces. The commoner parasites of meat and fish are listed in tabular form with remarks on each species. There is a host-parasite list of the species dealt with in the text. At the end of the volume are a series of outlines of the common helminth eggs, drawn to show relative sizes, and twelve large diagrams which set out in a very striking and simple manner the essential stages in the life-cycles of the more important forms. The authors have avoided overburdening the text with unessential terms and unimportant species, and the student's only regret will be that in so succinct and admirable a guide nothing is said of those arthropod parasites with which he has also to become familiar.

THE LANCET

LONDON: SATURDAY, AUGUST 20, 1938

THE PROGRESS OF HEALTH INSURANCE

In the report of the Ministry of Health issued last week [1] occasion is taken to review the progress of the national health insurance system during the first twenty-five years of its existence; and though the facts are briefly stated they suffice to show how enormous is the part played by the system in the life of the community. The number of insured persons in England and Wales, which was 11½ million at the outset, increased to over 17¾ million at the end of 1937, forming over 40 per cent. of the total population. The number of insured persons thus increased by more than 6¼ million, whereas the increase in the total population was not quite 4¾ million. In the twenty-five years the sum of £565 million has been expended in the provision of benefits—£202 million in sickness benefit, £94 million in disablement benefit, £35 million in maternity benefit, £194 million in medical benefit, and £40 million in additional benefits, the most important of which take the form of payment of part or the whole of the cost of dental or ophthalmic treatment. The financial position of the health insurance system has grown year by year in strength. The accumulated funds in England and Wales have steadily increased; at the end of 1937 they amounted to £123,654,000, and the interest on investments was £5,533,000. In view of such facts it is surprising to find that the English system of health insurance has been adversely criticised in America on the ground that it is heading for bankruptcy.

In 1925 health insurance was supplemented by the Widows', Orphans', and Old Age Contributory Pensions Scheme, which applied to all persons insured under the health insurance scheme. The total number of pensions now being paid is over 2½ million, about 721,000 to widows, 1¾ million to old-age pensioners, and about 255,000 in respect of children. The annual amount now paid in pensions under the contributory pensions scheme is about £40 million a year. The report remarks that:

> "An indication of the sense of social security engendered by this scheme may be found in the striking fact that three persons out of every four would be entitled, should the necessity arise, to receive old age, orphans' or widows' pensions—the latter also including allowances for children."

During 1937 the most noteworthy feature of the progress of health insurance was the extension of medical benefit, as from April of this year, to boys and girls insurably employed between the ages of fourteen and sixteen. Since these "juvenile contributors" are not entitled to sickness or disablement benefit they do not need certificates of incapacity for work, but otherwise the medical services provided for them are the same as for adults. For these boys and girls, who are estimated to number about a million at the outset, the gap between the school medical service and the insurance medical service will be bridged; and continuity of medical history is facilitated by the provision of the new Act under which an insurance doctor can, on application to the local education authority, obtain from the school medical officer information from the school medical record of any person under the age of eighteen whom he has accepted as an insured patient. The new Act marks an important forward step, not only because it brings a million young workers under the care of the insurance medical service but because it seems to foreshadow the more general extension of medical benefit for which the British Medical Association has long been pressing.

Another important development of the insurance medical service recorded in the report is the extension of the scheme for providing post-graduate study for insurance doctors. When the scheme was instituted over ten years ago it applied only to doctors practising in isolated rural areas who were unable from their own resources to afford the expense involved in taking a post-graduate course, but it has now been expanded to enable all doctors with a substantial number of insured patients to take courses of post-graduate study at five-yearly intervals. Urban as well as rural doctors are now eligible, irrespective of income, for post-graduate grants, which cover the course fee, travelling expenses and subsistence allowance, and where necessary the cost of a whole-time locum tenens. This year arrangements have been made, in consultation with the Insurance Acts Committee of the British Medical Association, for over 800 insurance doctors to take post-graduate courses in various medical schools in London and the provinces, and it is hoped that in the next year or two the number will be raised to a maximum of 2000 doctors a year. This development of the insurance medical service, though instituted primarily for the benefit of insured persons, should benefit the health of the whole population, for the insurance doctors constitute the great majority of the general practitioners of the country. It is an instance of how national health insurance may be made a means of enhancing the efficiency of medical practice. Twenty-five years ago there were many practitioners who thought that health insurance would degrade the standard of practice, and therefore would be bad for both the profession and the public, but experience has shown that, in this country at all events, it has had the contrary effect. That there has been a substantial advance in the standard of general practice during the last twenty-five years will hardly be doubted by any competent observer whose memories of practice go back to the days of the sixpenny doctor and the 4*s*. capitation fee of club practice; and though

[1] Nineteenth Annual Report of the Ministry of Health. 1937–38. H.M. Stationery Office. Cmd. 5801. Pp. 318. 5*s*.

various causes have contributed to this result a place must be accorded to the assumption of public responsibilities by the medical profession through the insurance medical service.

In one respect, however, the section of the report devoted to health insurance is disquieting; taking the medical service as a whole, increasing reliance seems to be placed on drugs as a means to health. The average number of prescriptions issued per insured person rose from 4·72 in 1936 to 4·75 in 1937 and the corresponding cost from 3*s.* 1½*d.* to 3*s.* 2*d.* The average ingredient cost per prescription rose from 3·784*d.* to 3·949*d.*, partly because of the growing use of new and expensive drugs. The report states that in some cases the treatment of one patient had cost no less than £240 a year in drugs alone. It was hoped that the working of national health insurance would bring about a material reduction in self-treatment by the use of patent medicines, but that has not been so. The craving for self-drugging is skilfully fostered in the advertisement columns of the popular press, and the medical profession is not to blame for it, though practitioners may do much to check it by health education among their patients. For the increased use of drugs in the insurance medical service, however, insurance doctors have a direct responsibility, both in their individual capacity and collectively through the agency of the panel committees. It is a characteristic of the English health insurance system that it invests the insurance practitioners with administrative responsibilities. Among them is the control of excessive prescribing, and the public is entitled to expect that the responsibility will be fulfilled.

PATIENTS IN THE AIR

PRACTITIONERS are already becoming familiar with the question: Is it safe for me to fly? The activities of our late Minister of Health—who seems as energetic in imperilling human life as he formerly was in safeguarding it—are bound to increase the number of those who expect their doctors to know the answer.

The effects of altitude experienced in an aeroplane differ in several ways from those experienced on high mountains. The element of acclimatisation is greatly lessened, and that of speed and variations in speed is added. As SCHLOMKA [1] has pointed out, the possible evil results of flying may be divided into those that arise from oxygen-want and those that arise from centrifugal force. The former are now fairly well known through the researches of laboratory workers and of the medical members of Everest expeditions. They can, of course, be wholly overcome by the use of oxygen apparatus, but such apparatus is not available in every aeroplane. In its absence the passenger is subjected to a low partial pressure of oxygen without any previous acclimatisation and will have to bear the weight of several maladjustments. He may suffer from tachycardia and dyspnœa through simple oxygen-lack. This is an inconvenience that may be serious in cardiovascular disease, for DIETRICH and SCHWIEGK [2] have shown that (as might be expected) anoxæmia affects patients suffering from myocardial or coronary disease far earlier and more seriously than it affects sound-hearted people. At the same time GILLERT [3] has drawn attention to the fact that expansion of intestinal gas, due to diminished atmospheric pressure, occurs even if oxygen is administered. The gas forces the diaphragm upwards, displaces the heart to the left, and interferes with the normal pumping action of respiration in moving blood from the inferior vena cava into the right auricle. This may be of little or no moment to the healthy man but may be serious for the invalid. Although complete acclimatisation cannot take place, it is possible that on the longest flights there may be a certain increase in the viscosity of the blood (SIROTINE [4]), and the repercussions of this on an inefficient heart cannot entirely be neglected. Nor must possible psychic effects be forgotten, for even the experienced air traveller may suffer from excitement on taking off and landing—though he may be loth to confess it. The possible nausea and vomiting of the bad "sailor" may itself be an important factor in deciding whether or not a particular person should be allowed to fly.

Of less importance in civil aviation is the influence of centrifugal force. By ordinary mathematical rules it is obvious that in those sudden changes of direction that are essential to aerobatics, but may occasionally happen in emergency even in a civil flight, the blood must be displaced violently towards the periphery. This often means a rush of blood to the feet and a depletion of the cranial supply. Elaborate experiments with dogs by KOENEN and RANKE [5] have shown that if the centrifugal force is more than 4 times gravity, the blood pressure in the carotids is permanently below zero. FISCHER, [6] using apes in his experiments, demonstrated radiographically that the heart became bloodless when the centrifugal force was increased to 4–4½ times gravity. These figures correspond with practical experience, for pilots find that a dimming of vision and unconsciousness occur at about the same point if the acceleration is maintained for more than about five seconds. According to the observations of BÜHRLEN, [7] if swinging seats were fitted it would be possible for aeroplane crews to withstand for a minute or more accelerations of 15 times the pull of gravity. Such seats may one day be provided in civil planes. At present, however, in considering the fitness of a patient for flying, it is wise to remember not only the effects of excitement, nausea, decreased atmospheric pressure, and oxygen-lack, but also the possible results of a sudden emigration of blood from the brain or thorax under the influence of centrifugal force.

[1] Schlomka, G., *Med. Klinik*, 1938, **34**, 421.

[2] Dietrich, S., and Schwiegk, H., *Z. klin. Med.* 1933, **125**, 195.
[3] Gillert, E., *Med. Klinik*, 1938, **34**, 423.
[4] Sirotine, N. N., *Médecine expérimentale* (Ukraine), 1937, **2**, 32.
[5] Koenen and Ranke, *Luftf. med.* 1937, **2** (quoted by Schlomka).
[6] Fischer, *Ibid*, 1937, **2** (quoted by Schlomka).
[7] Bührlen, *Ibid*, 1937, **1** (quoted by Schlomka).

TESTIMONIALS

ABOUT five years ago Dr. ROBERT HUTCHISON was asked four times in one week to write testimonials. Some of the applicants had passed through his wards as clerks several years previously, and he had forgotten them. The sequel was a Hutchisonian protest to the *British Medical Journal*.[1] All testimonials, he said, like funeral orations, are *bunkum*; "well may their writers exclaim with the Prophet: 'Who hath believed our report?'" Had the time not come to abolish testimonials for hospital appointments altogether and to judge candidates solely by their record and on the strength of a personal interview? In the correspondence that followed it was made abundantly clear that testimonials are dull and undifferentiated documents, distasteful to ask for, tedious to write, and destined to be ignored by those to whom they are addressed. The subject was reopened in the same correspondence columns last December, this time by surgeons complaining about the time and money wasted in the formalities of applying for appointments; one of them found the testimonial farce reminiscent of the giving of a "character" to a retiring maid-servant.[2] The obvious suggestion was made that hospitals and electing bodies should cease to ask for testimonials but should invite confidential opinions from referees on those candidates whose general records earn them a place on a short list.

With the maid-servants this has been the practice for a long time; a maid's reference consists of a name and a telephone number. And now at last one branch of the medical profession has followed the domestic example. The British Institute of Radiology and the Society of Radiographers have made a bargain[3] that no radiologist shall give, and no radiographer need ask for, an open testimonial. A standard certificate of radiographic employment is provided instead; it is a plain statement of experience. The radiologist is to give his opinion of the radiographer's ability and character only in the form of a confidential report to another radiologist or an electing body. Our X ray colleagues are professionally perspicacious and we wish all success to their new arrangement. It will be interesting to observe how slowly the reform spreads to medical appointments proper.

A voice here and there will probably defend the testimonial. In the benevolent glow of parting with a house-man who hasn't been so bad after all, the well-disposed chief will write him a better, perhaps a truer, recommendation than a year or two later when he has faded a little from memory. If access to the short list is to depend only on a bald statement of appointments held, the brilliant but little known man may remain little known. These difficulties should not be insuperable. Others with a taste for subtleties in English style will regret the passing of the really skilful testimonial in which the bearer can see nothing but faint praise while the recipient reads damnation between the lines. But how few testimonial-writers are capable of such gems! Certainly there are not enough of them to justify the dullness, or the fullsomeness, or the obliquity of all the rest. Such documents indeed, considered critically, often reveal more about the character of the describer than of the described: the classic and extreme example is from a member of a hospital staff who began, "Seldom have I written a testimonial with greater sincerity than I do for . . . ." This observation suggests the one basis on which testimonials might reasonably be retained—namely, that they be written by the junior on the subject of his chief. When Mr. Smith finishes his house appointments and applies for a registrarship let him write three testimonials for three of his chiefs and send them in with his application. They will tell quite a lot about Mr. Smith, and they will not be thumbed over unread at the staff meeting.

[1] *Brit. med. J.* 1933, 2, 843.
[2] *Ibid.* 1937, 2, 1200.
[3] *Brit. J. Radiol.* August, 1938, p. 505.

INTESTINAL INFANTILISM

APART from the syndrome of infantilism associated with disturbances of the endocrine glands and with chronic renal disease, it is known that malnutrition from the results of intestinal disease may play a part in inducing such a condition. Grossly defective absorption attributable to chronic mesenteric tuberculosis and cœliac disease, and defective secretion and absorption by the mucous membrane following acute gastro-enteritis and infantile ulcerative colitis may lead to retarded growth in children. It is not perhaps generally recognised that the localised infection of terminal ileitis (Crohn's disease) may cause a severe retardation of physical growth if the onset of the disease occurs early in the patient's life. One of the first cases recorded was that observed by Prof. I. SNAPPER and two colleagues[1] in a boy of 16 who had not grown after he became affected by the disease at the age of 9 years. The symptoms were those of attacks of diarrhœa; the motions contained no blood or mucus, no amœbæ or pathogenic micro-organisms were discovered, and the appearance of the patient and his fatty stools suggested Gee's disease. Radiography demonstrated a lesion of the terminal ileum and at operation a characteristic involvement of terminal ileum, cæcum, and ascending colon was found. It was not possible to resect the mass, so an anastomosis short-circuiting it was performed and a rapid recovery followed with increase of weight to normal.

A second case with almost parallel history has been recently reported from the Mayo Clinic.[2] A girl of 16 had had symptoms for three years, had lost 1½ st. in weight and remained undernourished and undeveloped. A barium enema revealed a granuloma of the ileocæcal region with patchy distribution of ulcerative ileitis involving the terminal portion of the ileum. An operation of ileocolostomy was performed, and in eighteen

[1] Proceedings of Second International Congress of Gastro-enterology, Brussels, 1937, p. 935.
[2] *Proc. Mayo Clin.* May 25th, 1938, p. 335.

months she had put on nearly 3 st. in weight. In adults it has usually been found necessary to remove the portion of the bowel involved in the granulomatous process before complete recovery is attained, since a form of hyperchromic anæmia is likely to follow if an exclusion type of operation only is performed. The diseased portion of the ileum, even though short-circuited, appears to continue its toxic effect. Though terminal ileitis is a disease which predominatingly affects young people, its occurrence in children as a factor in retarding growth is not widely known.

ANNOTATIONS

VASOMOTOR CONTROL OF CEREBRAL VESSELS

THE vasomotor control of the cerebral vessels is of no small interest to the clinician, for he often invokes changes in their calibre as an explanation of symptoms; for example, the manifestations of migraine and hypertensive encephalopathy are commonly attributed to cerebral vascular spasm. Physiologists long denied the existence of direct nervous control of the cerebral vessels, maintaining that the cerebral blood-flow is governed solely by vasomotor reactions throughout the body. It is now established, however, that nerve fibres, both myelinated and non-myelinated, are present on the cerebral vessels in man, and Forbes and Cobb [1] have lately demonstrated the direct action of dilator and constrictor fibres in monkeys, dogs, and cats. Arteries of the pia were observed microscopically through a cranial window and seen to contract when the cervical sympathetic was stimulated; the reaction was homolateral and limited to vessels not less than 50 μ in diameter, and it led to only about 8 per cent. reduction in calibre—i.e., about a tenth of the extent of the reaction in skin arteries. Vasodilatation of rather greater degree could be produced in pial arteries after stimulation of the geniculate ganglion. The local application to the vessels of cocaine, procaine, and ergotamine tartrate prevented the vasoconstrictor reaction, while cocaine and atropine prevented the vasodilator reaction, indicating that sympathetic and parasympathetic nerves, respectively, are involved in the reflex. These important observations establish the existence of a direct cerebral vasomotor control in animals, but show that it is relatively weak, a much larger part being played by chemical agents, especially carbon dioxide. Forbes and Cobb conclude from their experiments that the cerebral vasomotor mechanism may influence the local and general blood-flow through the brain but is incapable of causing ischæmia.

BRONCHIECTASIS AND SINUSITIS

THE fact that bronchitis and bronchiectasis are often associated with sinusitis is a commonplace to laryngologists, but Walsh and Meyer [2] think it too little appreciated by general practitioners and by specialists in other fields. They share the prevailing opinion that sinusitis and bronchitis deyelop simultaneously during an acute infection such as influenza, and they hold that patients with bronchitis tend to get well unless the condition is reinforced by a chronic sinus infection. Meyer, with Quinn,[3] found some years ago that iodised oil passed into the anterior nares during sleep was demonstrable next morning in large quantities in the bronchi and pulmonary parenchyma, and similar results have been obtained by other workers. It is reasonable therefore to believe that persistent pulmonary infection leading to bronchiectasis can be maintained by continual reinfection from the nasal sinuses. Walsh and Meyer now report on the incidence of sinusitis in 217 patients with bronchiectasis admitted to the Wisconsin General Hospital from 1925 to 1936. Cases of congenital bronchiectasis and those due to foreign body are not included, and sinusitis was diagnosed only when there was gross pus in one or more of the sinuses. On analysis sinusitis was found in 145 (67 per cent.) of these patients; of these, 22 dated their disease from an attack of influenza and 19 from pneumonia, but the incidence of these illnesses in the medical history was greater than this although the patients had not related their symptoms to them. The extent of involvement of the sinuses was variable, and no relation was established between the degree of sinusitis and the severity of the bronchiectasis. It is important to note that most of the patients had no nasal symptoms. Bronchiectasis without sinusitis was commonly preceded by influenza, pneumonia, or other infection of the respiratory tract, and it must therefore be realised that it can occur without gross infection of the sinuses. In these cases the possibility cannot be excluded that a sinusitis may have cleared up, or may have persisted in minimal degree; also, disease elsewhere in the upper respiratory tract, as in the tonsils, may be a source of reinfection of the bronchi. Walsh and Meyer believe that treatment of the sinuses, as well as of the lungs, is imperative if good results are to be obtained and they think that if disease of the sinuses is recognised and treated in early bronchitis, bronchiectasis will sometimes be prevented.

[1] Forbes, H. S., and Cobb, S. S., *Brain*, 1938, **61**, 221.
[2] Walsh, T. W., and Meyer, O. O., *Arch. intern. Med.* June, 1938, p. 890.
[3] Quinn, L. H., and Meyer, *Arch. Otolaryng., Chicago*, 1929, **10**, 152.

PHYSIQUE OF THE ARMY IN 1838

Colonel D. T. Richardson has been inquiring into the physical standards required of recruits for the army of a century ago. His paper [1] is based on a volume published in 1839 by the then deputy inspector-general of army hospitals. Apparently it was only since 1802 that there had been any systematic medical examination of recruits in Great Britain and Ireland by officially appointed doctors, and it was a good many years before these latter were given any sort of central guidance as to the standards to be applied.

It is of course impossible to form an accurate comparative picture of the physique of the manhood of the nation a hundred years ago from such figures as are available in respect of the recruiting of the 100,000 men who formed the average strength of the British Army for the years 1819 to 1828. But it is interesting to note that the minimum height of recruits for the infantry was 5 ft. 5½ in. to 5 ft. 6 in. —more than 3 in. in excess of that required at that time in France. The mean height of recruits, we are told, was between 5 ft. 7 in. and 5 ft. 8 in.; and Colonel Richardson quotes from a contemporary note of an Irish company of ninety men recruited at Cork

[1] *J. R. Army med. Cps*, July, 1938, p. 1.

in 1807, which shows that their average height was 5 ft. 7 in. This would probably be found to be about 2 in. less than the average height of any ordinary unselected series of ninety 18-year-old boys from normal London working-class families to-day or at most of our public schools. The minimum weight required at 18 was 127 lb. 9½ oz.; and this again is probably at least 10 lb. less than the average weight of the modern working-class or public schoolboy of the same age to-day. From a list of the causes of rejection, compiled from figures relating to Dublin in the years 1827–28, it is somewhat surprising to see that the biggest single cause of rejection was varicose veins (not including varicocele), which were responsible for 28·6 per 1000. Diseases of the eye—apart from mere defects of vision—also loom large, and ophthalmia, corneal opacities, and cataract accounted for 21·5 per 1000 of rejections. In both these respects a general review of the present-day youth of the nation would almost certainly show a much more satisfactory state of affairs.

A grim picture, both in itself and in its reflection upon general army conditions, especially on foreign service, emerges from the account of malingering to win freedom from military service. Self-imposed corneal ulcerations and artificially induced cataracts were not uncommon. Swellings intended to simulate hernias were ingeniously contrived, and epilepsy, paralysis, and insanity were often feigned in spite of the condign punishments dealt out to the discovered malingerer. The almost total disappearance of true malingering in the army of to-day is evidence of a revolutionary change in the attitude of the country to its armed forces.

HÆMOPOIETIC PRINCIPLES IN LIVER

EVIDENCE is accumulating from many sides that liver contains a variety of hæmopoietic principles. The pioneer work of Minot and Castle showed that the liver fraction curative in Addisonian pernicious anæmia was formed by the action of an intrinsic factor secreted by the stomach upon an extrinsic factor supplied by the food. This extrinsic factor was found to be present in meat and in autolysed yeast products such as Marmite. Other types of megalocytic hyperchromic anæmia, notably that described by Dr. Lucy Wills in India as tropical macrocytic anæmia, were found to respond as well to autolysed yeast as they do to liver. It was suggested therefore that such anæmias were due to lack of extrinsic factor only, dependent upon deficient diet. Using the sort of diet that is common in Bombay Dr. Wills was able to produce a macrocytic hyperchromic type of anæmia in monkeys. This responded to marmite and to crude liver extracts like Campolon but failed to respond to anahæmin and Examen, the purest liver extracts available. In our present issue Dr. Wills, having extended her work on monkeys to human cases with tropical macrocytic anæmia, reports further important observations. She found anahæmin as ineffective in human beings as it was in monkeys, though the same patients responded well to cruder liver extracts later. Prof. L. E. Napier and his co-workers [1] in Calcutta have made similar observations in certain cases of tropical macrocytic anæmia but have found anahæmin active in other cases. They therefore hope, by the therapeutic test, to be able to arrange these numerous cases into different "groups with common ætiological, hæmatological, and/or clinical characters." Since one large group of cases fails to respond to a principle curative in Addisonian pernicious anæmia the condition cannot be due, as was originally suggested, to lack of the extrinsic factor necessary for the formation of this principle, but must be caused by the absence of a hæmopoietic factor present in crude liver extracts and in autolysed yeast. The nature of this substance is unknown. Dr. Wills has reason to believe that it is not B_1, B_4, lactoflavin, or nicotinic acid. It follows from these interesting observations that whole liver contains an even greater variety of hæmopoietic substances than had been suspected: those now differentiated are (1) the principle effective in Addisonian pernicious anæmia; (2) the principle shown by Whipple to influence secondary anæmia; and (3) this new factor to which tropical or nutritional macrocytic anæmia has been shown to respond. The suggestion made last year by Jacobson and Subbarow [2] that the pernicious anæmia principle can itself be separated into four component parts adds a further complication. It is clear at least that the influence of nutrition upon hæmopoiesis is extremely important. The immediate clinical bearing of this work is noteworthy; if patients with macrocytic hyperchromic types of anæmia fail to respond to pure preparations of liver it is essential to try cruder preparations before deciding that they are resistant to liver therapy.

[1] Napier, L. E., Das Gupta, C. R., Chaudhuri, R. N., Sen, G. N., Chaudhuri, M. N. R., Sen Gupta, P. C., and Majumder, D. N., *Indian med. Gaz.* July, 1938, p. 385; see also *Lancet*, July 9th, p. 106.

FAMILIAL PERIODIC PARALYSIS

THE remarkable metabolic changes in familial periodic paralysis were first noted by Allott three years ago [3] and a description of some of the biochemical changes was published in 1937.[4] It was found that attacks could be produced by giving 200 g. of glucose by mouth, by insulin, or more consistently by the employment of glucose and insulin together. The attacks were associated with a fall in serum potassium and spontaneous or induced attacks could be dramatically arrested by the administration of 12 g. potassium chloride by mouth. These results have been extended in a further paper by Allott and McArdle.[5] Attacks were consistently produced in two new cases by glucose and insulin, and in one by the administration of adrenaline; in all cases the attacks were associated with a fall of serum potassium and were terminated by the administration of potassium salts. The action of adrenaline was found to produce a fall in serum potassium in normal people as well as in sufferers from this disease, in agreement with the observations of Castleden,[6] and not a rise such as that described by D'Silva in animals.[7] In one normal person the serum potassium was lowered to 10 mg. per 100 c.cm. by repeated administration of adrenaline without any paralytic manifestations, showing that the low serum potassium alone is insufficient explanation of the symptoms. A potassium balance experiment showed that potassium is retained in the body during attacks; the hypothesis was put forward that the attacks are due to an abnormal demand of the muscles for potassium, and that the falls in serum potassium and in potassium excretion are secondary effects due to an attempt to meet this demand.

These conclusions have now received support from America and from Canada. Ferrebee, Atchley, and

[2] Jacobson, B. M., and Subbarow, Y., *J. clin. Invest.* 1937, **16**, 573.
[3] Allott, E. N., quoted by Walker, M., *Lancet*, 1935, **2**, 47.
[4] Aitken, R. S., Allott, Castleden, L. I. M., and Walker, *Clin. Sci.* 1937, **3**, 47.
[5] Allott and McArdle, B., *Ibid*, April, 1938, p. 229.
[6] Castleden, *Ibid*, p. 241.
[7] D'Silva, J. L., *J. Physiol.* 1934, **82**, 393.

Loeb [8] confirm the fall in serum potassium, the diminution of potassium excretion during attacks, and the effectiveness of potassium chloride in alleviating paralysis. The Canadian workers [9] also confirm the fall in serum potassium and the therapeutic value of potassium salts, though their patient responded more slowly to oral potassium than the English ones. They have also investigated the effect of potassium chloride intravenously in doses of 0·5 g. to 2·0 g. Their observation that the serum potassium does not rise during the period of partial recovery lends support to the hypothesis that there is for some reason an abnormal demand for potassium in the muscles of affected subjects. Both the American and Canadian workers noted a constant creatinuria, which the American group found to increase during attacks; in the Canadian case the production of attacks by glucose and insulin was inconstant and adrenaline did not produce paralysis. The choline-esterase level in the blood was normal in the Canadian case but subnormal in the American ones. Taken together, all these observations show that the attacks of paralysis are associated with an abnormal demand for potassium on the part of the muscles, but the "trigger" which causes this abnormal demand seems to vary between different subjects.

LIMITATION OF OPIUM PRODUCTION

IN pursuance of the policy of limiting the production of raw opium and the cultivation of the opium poppy, referred to in our issue of July 9th, some further advance by the Advisory Committee of the League of Nations can now be recorded. They recognise that the superabundant supply of raw opium leads to the clandestine manufacture of morphine and heroin in large quantities, and obstructs international efforts to bring about the progressive abolition of opium-smoking. Twice as much raw opium is admittedly produced as is needed for legitimate purposes, without reckoning the unrecorded output of China, Manchukuo, and Jehol whose crop "is estimated to be far in excess of the production of the whole of the rest of the world." The problem is complicated by the relatively new process of extracting the opium alkaloids from poppy straw, and this source will have to be included in any scheme of limitation of production. The committee contemplate drafting a convention which will require estimates to be furnished annually by governments of their needs for recognised purposes, defining the areas of cultivation. There would be allocation of approved amounts of exports and imports either by a quota system or by a free order system. In the latter case each importing government would specify the country whose opium they desire to purchase. Stocks would have to be limited to a fixed level both in the producing and the consuming countries; excessive stocks would be reduced over a period of years. The convention would also contain provisions for international control and supervision, and also for national control alike in the producing and the consuming countries.

There was general acceptance by the members of the committee (33 in number) of the principle of limitation, and their report, after submission to the Council of the League, will be sent to the several governments for their observations. Examples of the ingenuity of illicit traffickers have lately been exposed in Paris by the arrest of two smugglers in the act of conveying heroin packed in hymn-books and prayer-books. The total quantity of heroin confiscated in one of these cases was valued at £3400.

[8] Ferrebee, J. W., Atchley, D. W., and Loeb, R. F., *J. clin. Invest.* July, 1938 (Proc.) p. 504.
[9] Pudenz, R. H., McIntosh, J. F., and McEachern, D., *Ibid* (Proc.) p. 530.

DISTRIBUTION OF LYMPHATICS IN THE HUMAN SKIN

THERE appear to be good grounds for a re-examination of the anatomical distribution of the lymphatics of human skin. Among debatable points are the number and depth of lymphatic plexuses between the dermis and subcutaneous tissue, the presence or absence of capillaries in the dermal papillæ, and the existence of small separate independent unit areas of drainage within the different watershed regions. It is only by injection methods that lymphatic channels can be mapped out and in order to make them effective two conditions must be satisfied: (1) the injection mass chosen must be one which can be relied on to penetrate even fine capillaries and to be made visible in situ; (2) the material used must be in a fit state of preservation. It used to be laid down by the old anatomists that the material to be injected could be dead but not stone dead, and the fresher the better. Gilbert Forbes's recent injection experiments [1] fail to carry conviction because he has deliberately discarded this advice by using the lymphatics of fœtuses which had been allowed to putrefy in a warm place for 14–21 days. His idea was to take advantage of the ease with which gas-filled channels can be injected. An injection made under such conditions, however, is necessarily incomplete, since it gives a picture only of the larger draining channels. None of the injection mass is likely to penetrate to the periphery even when the vessels have no valves, for there is little possibility of displacing the gases of putrefaction. More suitable material was used by J. H. Gray,[2] who injected Thorotrast into skin obtained fresh from the post-mortem room or operating theatre. Although this solution is sufficiently fluid to penetrate fine vessels it is rather doubtful whether very small ones which contain little of the solution will be shown in radiograms. The same objection probably applies to Hippuran [3] which has so far apparently been used only to show up the larger vessels.[4] Gray does not discuss these difficulties and indeed his conclusions seem rather far-reaching in relation to the data.

It is of course open to doubt whether lymphatic capillaries of normal skin in either the living body or material recently removed from it can always be injected completely. Normal small vessels are closed. Unless they are very numerous or the investigator is lucky enough to penetrate one of them rather than a deeper channel, they are liable to escape observation. The illustrations of Hudack and McMaster [5] serve as a warning and a standard in this respect. They emphasise again the greater value of a positive over a negative result and provide a valuable yardstick for judging the reliability of any technique. In view of the many excellent techniques available to-day for lymphatic injection in the living subject it should surely be possible to inject either the skin of volunteers, or at least fresh operation material, with india ink, Hydrokollag, or dyes, and eventually to map out the lymphatics of the skin of the whole adult body.

[1] Forbes, G., *J. Anat., Lond.* 1938, **72**, 399.
[2] Gray, J. H., Thirteenth annual report of the British Empire Cancer Campaign, 1936, p. 34.
[3] Jaches, L., and Swick, M., *Radiology*, 1934, **23**, 216.
[4] Westhues, H., *Chirurg*, 1935, **7**, 370.
[5] Hudack, S. S., and McMaster, P. D., *J. exp. Med.* 1933, **57**, 751.

TREATMENT OF PHTHISIS BY INTRA-PULMONARY INJECTIONS

WHEN an authority of Fishberg's eminence declares that less than 5 per cent. of cases of pulmonary tuberculosis are suitable for collapse therapy it is not unnatural that phthisiologists should seek for other means of cutting short the lengthy treatment of the consumptive. Attempts to achieve this object by injecting chemical substances directly into the lung have lately been described in two journals.

Sir James Roberts [1] puts his faith in carbolic acid, and after trial and error now uses a strength of 1 in 64 carbolic made up in double the quantity of glycerin. With the aid of an X ray picture and a stethoscopy to reveal the most affected area, 1·0 to 1·5 c.cm. of the solution is slowly injected into the lung through the chest wall. The injection is repeated frequently in different parts of the lung, at first daily, and later two or three times a week as improvement becomes manifest. A course of such treatment might last from one to six months. The author claims that it does no harm to inject the fluid directly into a cavity but is actually beneficial in leading to contraction and obliteration. In India he has given 45,000 such injections without any untoward effects after the early experimental period when 2 patients collapsed and died as a result of using too strong a solution and too much of it. Although, according to Roberts, the disease in Indians assumes a form more acute and more rapidly progressive than it does among Europeans, he does not hesitate to use the word "cure" more freely than it is employed in this country, and he gives the results of 149 cases as 64 discharged cured with a negative sputum, a further 40 improved but unable to remain in hospital for the completion of treatment, 26 discharged as too advanced, usually because of a heavily infected abdomen, and 19 dead, the patients being moribund on arrival. He has not restricted the use of these injections to pulmonary disease but has used them in such non-tuberculous conditions as bronchiectasis, chronic rheumatic pains, lumbago, and osteo-arthritis, in all with apparent success. On the other hand Trowell [2] who tried the method in 15 moderately advanced cases and 1 early case of phthisis in African natives had such complete failure that he gave it up after six weeks, 4 of his patients dying and 8 getting worse, while the other 4 showed no change. Trowell comments unfavourably on deficiencies in the information given by Roberts and we share his opinion that no case has been made out in favour of phenol as a therapeutic agent for phthisis.

The other attempt at intrapulmonary injection is that of Hunter and Peill,[3] of the Bridge of Weir Sanatorium, who employ a solution of gelatin, acriflavine, and calcium chloride (G.A.C.C.). Their original G.A.C.C. contained 5 per cent. gelatin but they later increased this to 30 per cent. gelatin (G.A.C.C. "B") in the hope that the stronger and more "sluggish" solution would remain longer in a cavity and leave a thicker coating on its wall. They give in detail the formula for preparation of G.A.C.C. "B" which must be injected into the lung at a temperature of about 80° C. The rationale of the treatment rests upon the fact that gelatin acts on fibrous tissue, converting it into a hyaline state, calcification being induced by the addition of the chloride. A preliminary investigation of the effect of the compound when injected into the lungs of rabbits was undertaken, hyalinisation and calcification becoming apparent in the injected lung as compared with the control side. The experiment was extended to rabbits infected with the bovine tubercle bacillus with a gratifying slowing of the tuberculous process accompanied by increased fibrosis and calcification in the treated group compared with the untreated controls. They describe the technique used for injecting human beings and conclude, after giving 180 injections without accident, that it is safe provided care is taken to ensure that the point of the needle is not in a vein. An injection is sometimes followed by a reaction consisting in a rise of temperature and pulse-rate with malaise and anorexia, all of short duration. It is a preliminary report and exact details of the results are lacking, but the three cases recorded at some length, and the apparent safety of the procedure, seem to justify its further trial.

[1] Roberts, J. R., *East Afr. med. J.* 1937, **14**, 221, 251.
[2] Trowell, H. C., *Ibid*, March, 1938, p. 386.
[3] Hunter, R. A., and Peill, E. J., *Brit. J. Tuberc.* July, 1938 p. 136.

ISOLATION OF *BACT. TYPHOSUM* FROM SEWAGE

DURING the eighty years or so that have passed since Budd and others established the overwhelming importance of fæcal contamination of food and drink in the causation of the enteric fevers, it has been usual to trace successfully the source of enteric infection in water-borne and milk-borne epidemics by means of epidemiological detective work, to which the most important laboratory aid was the *Bacterium coli* test. The presence of *Bact. coli* in more than minimal numbers in drinking water was taken as presumptive evidence of fæcal contamination, and when such contamination was stopped the outbreaks usually ceased. With the progress of bacteriology it became possible to attribute special importance to the presence of certain varieties of coliform organisms. Thus what is now known as typical *Bact. coli*—which is Voges-Proskauer and Koser negative, a non-fermenter of inositol and a producer of indole—is particularly characteristic of human fæces and is therefore of special value in suggesting fæcal pollution, while *Bact. aerogenes* and certain other forms provide less definite evidence of human fæcal pollution. The direct demonstration of *Bact. typhosum* in waters and sewage was almost impossible by the laboratory methods available up to a few years ago, but the situation has been greatly changed by the work of Wilson and Blair,[1] who in 1927 introduced their bismuth sulphite medium for the isolation of this organism. Since 1928 *Bact. typhosum* has been successfully isolated from sewage on numerous occasions by means of this medium. Prof. Wilson himself recovered it from Belfast sewage in 1928, and later Gray [2] and Begbie and Gibson [3] obtained it from Edinburgh sewage, while the late Sir Alexander Houston [4] isolated it from the Thames. Since then further successes have been recorded by a number of workers both in Great Britain and in other parts of the world. In the current number of the *Journal of Hygiene* Prof. Wilson [5] most usefully sums up the situation with regard to the isolation of *Bact. typhosum* in water- and milk-borne epidemics and adds some valuable notes on his present technique for using the bismuth sulphite medium. He describes how he was able to isolate *Bact. typhosum* from a well of an

[1] Wilson, W. J., and Blair, E. M. McV., *J. Hyg., Camb.* 1927, **26**, 374.
[2] Gray, J. D. A., *Brit. med. J.* 1929, **1**, 142.
[3] Begbie, R. S., and Gibson, H. J., *Ibid*, 1930, **2**, 55.
[4] Houston, A. C., 23rd–26th ann. reports of the Metropolitan Water Board (1928–31).
[5] Wilson, W. J., *J. Hyg., Camb.* July, 1938, p. 507.

institution in which an outbreak of enteric fever had occurred and from a stream adjoining a well in a farmyard in Belfast at a time when the milk was the source of infection of over 100 cases of the disease. He also records the isolation of *Bact. typhosum* from a cesspool discharging into a stream near Bournemouth. In this last case it is suggested that a woman from whose premises milk was obtained, which was the infective vehicle in the Bournemouth-Poole epidemic, may have been a "precocious carrier." She died of typhoid but not before 29 other patients had fallen ill.

It is clear that Wilson and Blair's method provides a new and very useful means of investigation in enteric epidemics. It in no way replaces the *coli* test but where it is applicable the source of infection can be traced in much more precise manner than by any merely "presumptive" test.

NEW DRUGS AND THE AMERICAN LAW

THE authorities responsible for administration of the recently enacted law of the United States of America controlling the sale of foods and drugs have lost no time in preparing regulations under the section of the Act that prohibits traffic in "new drugs" unless they have been adequately tested to show that they are safe for use in the conditions prescribed in their labelling. The regulations provide that an application in respect of a new drug, to be valid, must contain full reports of investigations made; a full list of the articles used as components of the drug; a full statement of the composition of the drug; a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the drug; and specimens of the labelling proposed to be used for the drug. A new drug intended solely for investigational use by experts qualified by scientific experience to investigate the safety of drugs will be exempt from the operation of this section of the Act if its label bears the statement "for investigational use only" and provided precautions are taken to see that it shall be used only by an expert and for this purpose.

FUTURE OF MEDICAL WORK IN CHINA

IN an address delivered at Hong-Kong a few weeks ago Dr. T. D. Stevenson, of the Lingnam University medical college at Canton, examined the outlook for medical practice in China and the ways in which sound care can be provided.[1] Modern medicine, he said, is too expensive for the mass of the Chinese people, its high cost being attributable partly to the adverse money exchange, partly to the growth of a belief in injections, fostered by quacks and those who wish to get rich quickly, and partly to the prescribing of drugs under expensive trade names. To meet this situation Dr. Stevenson recommended that injections should be given only where necessary, that many of the remedies required for injection should be prepared in ampoules locally, and that drugs should be prescribed under their own names. He believes that national insurance or panel practice would be inappropriate for China and declared himself in favour of a system of State medicine. It will be generally agreed that for a country with vast rural areas, in which the farmers make the barest of livings, medical work must be based on a State service though private practice may be to some extent possible in the cities. The distances are so great, and the conditions in various parts of the country so different, that China is not strictly comparable with any Western country; and it would be useless to attempt any slavish copy of what has been successful in Europe.

[1] *South China Morning Post*, July 14th, 1938.

BROKEN NEEDLES

THE breaking of a needle was a more troublesome accident in the surgery of the past than it is to-day. Many who were house surgeons before X rays came into use will remember interminable hunts for the portion of a needle embedded in the palm of the hand or the sole of the foot. Location was precarious, dissection unguided, and the search, wisely postponed to an otherwise easy Sunday morning, protracted often for hours. Where radiography is available these labours belong only to the past; but with the increased frequency of injections of all kinds the needle broken by the doctor is now a commoner cause of trouble than the domestic needle trodden on or snapped off by the patient. With the aid of X rays the hunt is usually short and successful, but these accidents nevertheless have a kind of dramatic interest peculiar to themselves, and their consequences if untreated are not always negligible. This is well brought out in a paper in the July number of the *British Journal of Anæsthesia* by Dr. J. N. Cave. He confines his words to the breaking of needles used for spinal injection, but in this limited sphere he has collected a number of instructive examples. Curiously enough, in the first recorded case of a needle broken in the spine the breakage was not the result of an attempted injection but of the action of a small boy who threw himself backwards on a settee and drove a darning needle into his back. Pain in the legs developed and was relieved only after abstraction of the needle, which had been broken off by the vertebral arches. Dr. Cave considers the circumstances most likely to lead to the breaking of a spinal needle and thereby suggests ways of avoiding it. His paper may be read with advantage by anæsthetists and with interest by others.

THE OPERATIONS IN WAZIRISTAN

AMONG honours conferred for services rendered in connexion with the operations in Waziristan from September to December last year are the following:—

C.B.E. (*Military*).—Colonel R. E. U. Newman, O.B.E., M.C., M.B. Edin., R.A.M.C. (now retired).

D.S.O.—Lieut.-Colonel Stanley Arnott, M.D. Edin., R.A.M.C.

M.B.E. (*Military*).—Captain V. M. Albuquerque, F.R.C.S. Eng., I.M.S.

Military Medal.—Lieutenant (late assistant surgeon) M. C. Condillac, M.R.C.S. Eng., Auxiliary Force Medical Corps, India.

THE LANCET 100 YEARS AGO

August 18th, 1838, p. 722.

From a leading article.

THE verdict of the Somersetshire jury has recognised the culpability . . . but the amount of damages awarded fills us with astonishment; for low as medical labour has sunk we were not aware that the value of a pauper's arm in Bridgewater had fallen so low as *five pounds*. . . . Under the barbarous jurisprudence of the Normans injury was atoned for by pecuniary fines: the eye, the ear, the leg, the arm, the life were valued and the mulct effaced the crime; but it does not appear . . . that a lower price was ever set upon a human arm. . . . These ill advised and cruel measures will inevitably lead the people of Bridgewater to inquire what is the value of a Guardian's neck, where a woman's arm is valued at £5, and pauper's lives are weighed down by water gruel.

SPECIAL ARTICLES

THE DESTRUCTION OF MOSQUITOES IN AIRCRAFT

BY F. P. MACKIE, C.S.I., O.B.E., M.D., M.Sc., F.R.C.S., F.R.C.P., D.P.H.
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AIRCRAFT travel has introduced new problems into public health. Speed has obliterated the natural frontiers of disease in that epidemic and endemic areas are now brought into close contact with healthy areas and passengers may fly from the one to the other within the incubation period of all but the most fulminating diseases.

Apart from human passengers there is another danger—namely, from the possible transmission of infected insects which if conditions are favourable may start an epidemic in a new country.

The probabilities of transmission by either of these agencies vary in different diseases according to their natural history. Most attention has been directed to mosquito-borne diseases, particularly to yellow fever, and the observations described in this paper have been focused on this disease because it is one of the few great plagues which has never become pandemic and one which would bring disaster if it did. It is at the same time eminently suited for dissemination by aeroplanes.

Regulations laid down in 1933 in the International Sanitary Convention for Aerial Navigation were directed to the danger of mosquitoes in aircraft and the necessity for "disinsectisation" (Article 42), and since that time the matter has been repeatedly discussed by the quarantine commission of the Office International d'Hygiène publique. According to this convention, all responsibility in connexion with the aerial transport of disease lies with the sanitary authorities of the various countries through which the aircraft passses, not only in the inspection and quarantine regulations applicable to passengers but in the provision of "sanitary" or "anti-amaryl" aerodromes and in the measures directed against insect vectors at various stages of their life-history. At present all such measures are carried out by local sanitary authorities at the various airports and refuelling stations.

The aircraft of Imperial Airways on the south-bound service pass through the following countries in Africa: Egypt, Anglo-Egyptian Sudan, Uganda, Kenya, Tanganyika, Portugese East Africa, and Natal. On the service to West Africa they pass through Egypt, the Anglo-Egyptian Sudan, French Equatorial Africa, Nigeria, and the Gold Coast. Some of these countries contain endemic centres of yellow fever; others are regarded as suspect because mouse-protection tests have been found positive; others are regarded as potentially infected by reason of their geographical position; whilst others again are as yet free from the disease.

The problem that confronts the local government of each of these territories, as well as the aircraft company passing through them, is a complex one, and it is not surprising that confusion has arisen regarding the duties and responsibilities of the principal participants who are equally concerned to prevent the transmission of disease from one country to another. In practice it is found that some countries are seriously alarmed at the possible introduction of yellow fever and insist on carrying out, or demanding that others should carry out for them, every possible preventive measure. Some authorities, on the other hand, are less exacting and are satisfied if the minimum measures demanded by the Convention are observed, whilst if a country refuses to subscribe to the requirements of the Convention there are no powers to ensure its compliance.

DISINFESTATION IN FLIGHT

It was obvious to us at an early stage of our investigations that the best way to overcome our difficulties and to ensure effective compliance with the Convention's requirements was to perfect a system for disinfestation in flight.

It must be remembered that there is an ever-extending network of air-lines in Africa—and apart from occasional unscheduled landings a large number of small refueling stations are springing up in undeveloped country where there is no ground organisation capable of efficient disinfestation. The requirements of the Convention, whether applicable to regular air-lines, to military aircraft, or to private aeroplanes, would be equally well served by disinfestation during flight and we consider this to be the method of the future, at any rate for organised commercial services.

During our work we have been in close touch with Dr. Park Ross, deputy chief health officer of the Union of South Africa. The convergence of aircraft from known endemic areas in Africa has impressed on the Union Government the urgent need for yellow fever control and credit is due to Dr. Park Ross and his advisers for the advance they have made. We are also indebted to him and to Mr. Larmuth of the South African Fumigation Company for a simple and economical method of spraying by the use of a carbon dioxide Sparklet apparatus the details of which are given below.

THE CHOICE OF AN INSECTICIDE

We first considered the use of a gaseous insecticide which could be pumped into a closed fuselage and subsequently blown out by the ventilation system. Of the gases which might be used hydrocyanic acid and others, like ethylene oxide and methyl bromide, require further study. The length of time involved in such operations is an additional objection to their use.

The large majority of insecticides now in use depend for their toxicity to insects on pyrethrum (which acts as a neuromuscular poison) or its derivatives. This is generally dissolved in a paraffin base with or without tetrachloride to reduce inflammability. One such in common use is composed of: pyrethrum extract, 1 part; low-flashpoint white paraffin, 16 parts; and carbon tetrachloride, 68 parts.

The ideal insecticide for aircraft work should be: (*a*) highly toxic to insects; (*b*) non-inflammable; (*c*) innocuous to passengers; (*d*) non-corrosive and non-staining; (*e*) stable in the form used for transport and storage; and (*f*) miscible with water and adapted to spraying. It is obvious that paraffin-base insecticides do not conform with (*b*) and the addition to them of carbon tetrachloride produces undesirable

effects, such as headache, sore-throat, smarting of the eyes and nose, and vertigo. This would not matter where aircraft is disinfected on the ground, but when the process is carried on during flight, passengers and crew are exposed to the vapour.

The risk of fire is of great importance in aeroplanes, and even when inflammability is reduced or damped down by carbon tetrachloride the repeated application of a paraffin-containing fluid slowly saturates cushions and textiles and in time renders them highly inflammable.

It is true that some of the paraffin-base insecticides will not take light when in bulk, but when sprayed on to a live flame or hot metal they will flash back to the nozzle. Hence the presence of paraffin at various points throughout the fuselage would be an added risk in case of fire. For those reasons we have been forced to concentrate our attention on aqueous-base insecticides and we have come to the conclusion that, of the samples so far tested, Messrs. Stafford Allen's Deskito, a watery-base pyrethrum insecticide conforms most closely with the above requirements.

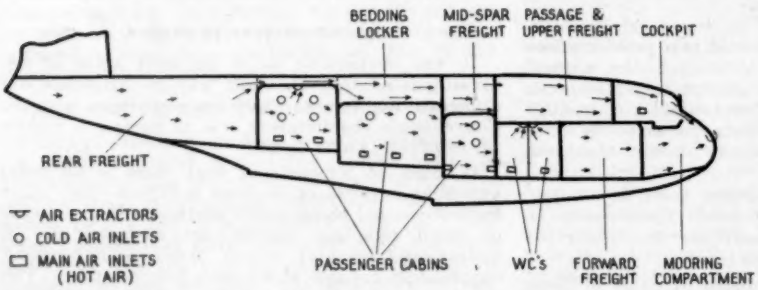


FIG. 1.—Ventilation of an Imperial flying boat.

THE SPRAY APPARATUS

It was proposed at one time to set up a system of tubes throughout the aeroplane in imitation of the tracheal system of an insect's respiratory apparatus, but it was found that a gaseous insecticide would have to be used and from a commercial point of view the weight of such an apparatus would be prohibitive.

The sanitary authorities in different countries use a variety of pressure sprays, from the domestic Flit gun to powerful pumps operated electrically. The diffusibility and penetration of the insecticide vapour, and therefore its effectiveness, vary accordingly to the type of gun used. The apparatus used in our experiments was Larmuth's device, driven by the pressure of CO_2 in a sparklet bulb, and for the passengers' cabins the Phantomyst nebuliser, made by Messrs. Andre (Components) Ltd. Experiments with aqueous-base insecticide projected by Larmuth's device and by the phantomyst having proved satisfactory, it was decided to fit up a flying boat with a demonstration outfit and to invite sanitary authorities on the route between Cairo and Durban to witness the procedure and give us their views. Before giving details of these flights a few remarks regarding the engineering side of the problem are necessary.

THE AIRCRAFT AND THE APPARATUS

Successful disinfestation in the air depends on the ventilation system carried by any particular type of aircraft. A disinfestation apparatus carried by one type would not necessarily be effective if placed in a second type, owing to difference in the ventilation system.

Ventilation system of the Imperial flying boat.—This aircraft (Fig. 1) is divided into two decks. On the lower deck the passenger carrying portion of the aircraft has three separate air systems which together make up the ventilation system: (i) the main air inlet system; (ii) the cold air system (punkah louvre); and (iii) the extractor system. The temperature of the main air can be varied, but the quantity cannot be altered. The cold air system is controlled in the cabins through punkah louvres which can be shut off. The extractor system operates four extractors. The three major extractors are located one in each of the lavatories and one in the galley. The fourth is a small volume extractor in the smoking compartment.

On the upper deck there is only one supply of hot air in the control cabin. There is, however, a very marked drift of air from the rear freight compartment of the aircraft through the bedding locker to the control cabin. The speed of the drift is slow, and is due to the aerodynamic forces exerted by the outside air flow over the hull. This same air drift is also noticeable through the cabins of the aircraft. The drift is not affected by shutting off either extractor system or cold air system.

The wings of the Imperial flying boat are well ventilated by a large volume of fresh air moving at a fast speed. (There is no record of live mosquitoes having been found in the wings of an Imperial flying boat.)

Description of apparatus.—The apparatus used (Figs. 2 and 3) has been developed specially for the Imperial flying boat. The apparatus is divided into two separate systems.

(*a*) A disseminator specially designed to disseminate "dry" insecticide in the passenger cabins.

(*b*) "Ejector" type disseminator suitable for all luggage holds, bedding lockers, &c., and all parts of the aircraft other than the cabins.

The first is the phantomyst apparatus already mentioned, which has been specially developed for use in aircraft. This machine is driven electrically from the flying boat's electricity supply, and is carried from cabin to cabin. The mist which it disseminates is termed "dry," the size of the droplets being of the order of 6μ, and no condensation of the mist is noticeable. The machine has been calibrated and disseminates a given quantity of insecticide per minute. Attached to the machine is a label giving the length of time the machine should be run in each cabin.

The ejectors are a simple form of spray gun operated by a sparklet bulb as designed by Mr. Larmuth. Each has a container calibrated to hold 50 c.cm. of insecticide. This container has a quick-action threaded collar at its top end, and screws into the operating head of the ejector. From the operating head a small copper pipe leads away into the particular compartment, where two or more fine jets are located. In all instances it is possible to fill and fire each ejector in the air without entering the compartment which is to be disinfested.

The total weight of the equipment as installed in the Imperial flying boat *Cassiopeia* is 32 lb. Six of the ejectors are located in the aircraft.

Disinfestation in flight.—Immediately after take-off the ejectors, which have been filled with diluted insecticide while the aircraft was at rest, are fired throughout the aircraft. The phantomyst apparatus is then taken into the rear cabin and switched on. For ten minutes this apparatus is run in the rear cabin. During this time the cold air punkah louvres are kept shut. It should be remembered, however, that there is still hot or cold air (according to the temperature of the cabins) entering the cabins through the main air system. With the exception of the small extractor in the rear smoking cabin, the extractor system is blanked off.

Cabin or compartment.	Capacity (cubic feet).	Disinfested by—	Ejector head located by—	No. of c.cm. disseminated.	No. of jets.
LOWER DECK. Mooring compartment.	287	Ejector.	Forward bulkhead of forward freight.	50	2
Forward freight.	480	Ph.*	..	14	—
Galley and w.c.'s.	480	Ph.	..	14	—
Mid cabin.	480	Ph.	..	14	—
Promenade cabin.	992	Ph.	..	21	—
Rear cabin.	763	Ph.	..	14	—
Rear freight.	1290	Ejector.	Rear wall of rear cabin.	50	3
UPPER DECK. Cockpit and cockpit passage.	618	Ejector.	Starboard side of partition between passage and upper freight.	50	2
Upper freight.	300	Ejector.	Ditto.	50	2
Mid spar.	300	,,	Ditto.	50	2
Bedding locker.	331	,,	Forward wall of rear cabin.	50	2

* The phantomyst (Ph.) apparatus developed for use in aircraft was set to disseminate 1·4 c.cm. of deskito per minute (dilution 1 part of deskito to 10 parts of water).

After 10 minutes the phantomyst is removed to the promenade cabin, where the cold air punkah louvres are shut and the apparatus is allowed to run for 15 minutes. (It is possible to open punkah louvres in the rear cabin immediately the nebuliser has been removed.) This same procedure is adopted for the mid cabin, galley and forward cabin, the total length of time being 55 minutes.

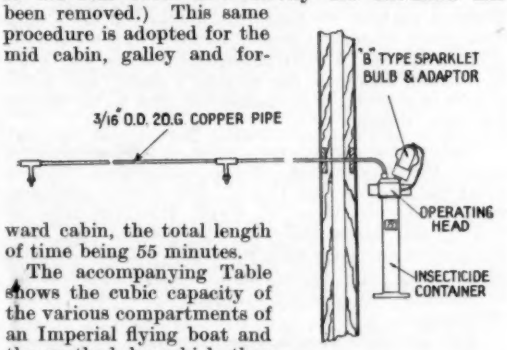


FIG. 3.—Ejector system.

The accompanying Table shows the cubic capacity of the various compartments of an Imperial flying boat and the method by which they were disinfested (see Figs. 1 and 2).

EXPERIMENTS

The following is a summary of the experiments which have been carried out. Full details may be obtained on application to Imperial Airways Ltd.

Expt. 1 was made in test chambers of known capacity. Mosquitoes were killed within 8–13 minutes after exposure to 18 c.cm. of 1 in 14 deskito in a space of 1100 cubic feet.

Expt. 2.—Preliminary experiments proving satisfactory, the flying boat *Cassiopeia* was fitted up with ejectors and nebuliser and flew on her normal service from Southampton to Durban via Cairo, Khartoum, Kisumu, and the East African ports. The disinfesting procedures were carried out by First Officer Stroud and demonstrations given by him to the government sanitary authorities at the places named. These demonstrations were on the whole very successful and were favourably commented on by the majority of observers. It was suggested that air currents set up in flight might alter the efficacy of the insecticide and it was agreed that on the next occasion disinfestation should be carried out during flight.

A few minor defects were noted either in the structure of the apparatus or in the method of using it, but with experience these were readily overcome. Dr. Park Ross was not altogether satisfied with the speed and completeness of the kill with deskito and found that his own preparation "aircraft pyagra" was more satisfactory. Unfortunately this is a paraffin-base insecticide; moreover it gave rise to

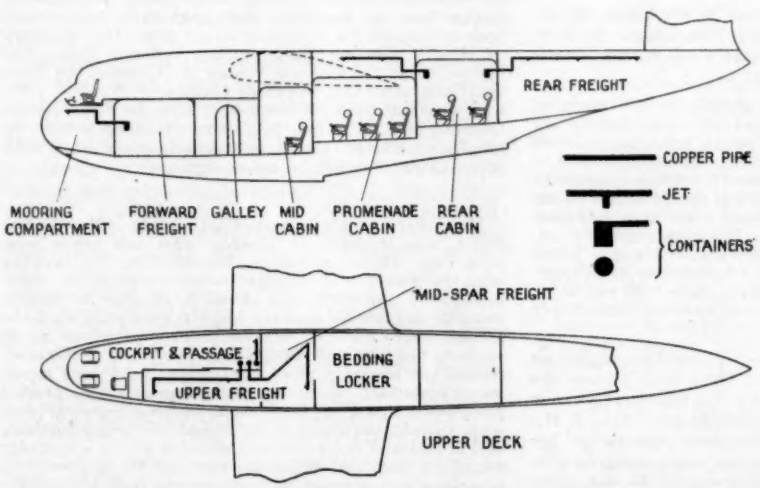


FIG. 2.—Location of insecticide ejectors.

unpleasant after-effects in those exposed to its vapour.

Expt. 3 was carried out on the flying boat *Cambria* whilst in flight over Southampton in order to test the influence of air currents at different altitudes and to assess the value of the principle of "disinfestation in flight." This experiment was entirely successful; the caged mosquitoes, which were placed in the different parts of the aircraft as detailed in the Table, were killed in periods from 2 minutes to a maximum of 11 minutes. A control cage of insects was kept in a sealed locker in the steward's galley and these insects were found to be unaffected after all the others had been killed.

Expt. 4 was carried out under similar conditions under the observation of the authorities referred to at the end of this paper. The results obtained were similar to those of Expt. 3 except that in two of the cages the kill was delayed and two mosquitoes survived until next day. These defects, which were due to mechanical causes introduced to simplify the ejector system, have been easily remedied.

Since our experiments were completed two reports have come in from independent authorities.

Expt. 5.—The first is from C. B. Symes, the government entomologist of British East Africa whose work on insects and aircraft is well known.

He used a furnished room of 1920 cubic feet and a dose of 28·5 c.cm. of 1 in 14 deskito. Fourteen species of mosquitoes were used including culex, aedes, and anopheles. The cages which were placed in various positions in the room were exposed to the vapour for five minutes after which all were removed to fresh air.

Mr. Symes's conclusions were as follows: (i) over half of the specimens were brought down in 5 minutes; (ii) after 5 minutes in the open air another 33 per cent. were rendered incapable; (iii) none were capable of flight after 30 minutes (i.e., 25 minutes in the open air); and (iv) there were no recoveries. Some appeared to be only slightly affected during the 5 minutes' exposure but all succumbed within the half hour.

These experiments are interesting in showing the delayed action of pyrethrum and also in showing that some insects which appear to be unaffected have actually received a fatal dose. This has been noticed in our own experiments.

The latest report is from Prof. J. W. Munro of the Imperial College of Science and Technology, London, who has kindly permitted us to refer to his results before their publication in full.

He states that the dosage should be 150 c.cm. of 1 in 30 deskito in water per 1000 cubic feet of air space and that there should be 15 minutes' interval between spraying and ventilation. He used batches of *Culex fatigans* in groups of 50–70. After treatment they were kept under observation for 24 hours to see if any recovered. It was found that in a chamber of 600 litres capacity 3·0 c.cm., 2·5 c.cm., or 2·0 c.cm. of insecticide killed all the insects, 1·5 c.cm. killed 99·5 per cent., 1·0 c.cm. killed 97 per cent., 0·75 c.cm. killed 88 per cent., and 0·5 c.cm. killed 76 per cent. The mortality of control insects was less than 6 per cent.

Prof. Munro concludes that provided the conditions of control in aeroplanes do not differ widely from the laboratory conditions (in which the temperature was 23°–24° C., and the humidity 30–40 per cent. R.H.) deskito should prove a satisfactory insecticide for most mosquitoes. At the higher temperatures met with in the tropics its efficiency should be enhanced provided the pyrethrum content is not altered.

REMARKS

The potency of pyrethrum in a finely divided state is remarkable and it is difficult to believe that the almost invisible vapour has diffused so quickly as to reach insects even in sheltered positions and kill them so quickly. It is interesting to notice that the first impact of the vapour stirs mosquitoes into activity so that they fly wildly from side to side of the cage before they begin to drop. If this reaction is constant it will be advantageous, for it will bring them out of partially protected hiding places and thus expose them to a higher concentration of the insecticide.

We noted that the action of the vapour is delayed and irreversible; in every cage there would be one or more insects still active when the rest were dead, but once down they never recovered. Mr. Symes's observations bring out this point very clearly. The same was noted in the Experiment 4 where, owing to some mechanical or ventilation defects some insects were found to be alive at the conclusion of the experiment. An hour or so later (having meanwhile been in the fresh air) they were found to have died.

Another point of interest is that although there is a constant slow forward drift of vapour when the aircraft is in flight, the mosquitoes placed far back in the tail were readily killed, though no spray jet was in the vicinity and the natural drift would have been away from the cage.

CONCLUSION

We do not claim that we have perfected this method, but we believe that disinfestation in flight is, for the reasons we have given, the method of the future for cabin type aircraft. Imperial Airways Ltd. proposes to fit out some of the flying boats on the Empire routes with this insecticide apparatus and invites local sanitary authorities to satisfy themselves that in practice this method results in the complete destruction of mosquitoes. We realise that the final responsibility for insect destruction in aircraft rests with the ground sanitary authorities, but we hope that with a perfecting of this method a certificate of disinfestation from the aircraft commander will be accepted, and that both punctuality and speed, the essentials of air travel, will thereby be ensured.

We have benefited from the advice and criticism at different stages of the work from well-known authorities in London, and our last experiment was witnessed by representatives from the Ministry of Health, the Air Ministry, the Colonial Office, the India Office, the London School of Hygiene, the Ross Institute, and the Imperial College of Science. We are most grateful to them and also to Sir Rickard Christophers, F.R.S., professor of malariology in the University of London, who kindly supplied us with mosquitoes and helped us in other ways.

HOSPITALS FOR AIR-RAID CASUALTIES.—Mr. Walter Elliot, the Minister of Health, who has taken over from the Home Secretary responsibility for dealing with the provision of hospital accommodation for those injured in air raids, has issued a circular to county councils and county borough councils explaining that the Ministry are working out comprehensive plans which could be put into operation in various parts of the country should the necessity arise. Although the details would vary according to local circumstances, the general principle is that every hospital must be prepared to deal with air-raid casualties in its immediate neighbourhood, and in addition every hospital which is not in a specially dangerous position would be expected to receive both casualties and ordinary patients moved from the danger areas.

ŒSTRIN EXCRETION IN THE URINE OF NORMAL WOMEN

A NOTE by Spurrell and Ucko,[1] from the physiological laboratory of Guy's Hospital, discusses the practicability of urinary œstrin assays as a liaison service to an endocrine clinic. They find that, in the normal menstrual cycle, morning specimens of urine show much the same variation of œstrin excretion as is shown by 24-hour collections. After receiving this encouragement, however, they have come up against the difficulty of fixing on a "normal" excretion curve, and they conclude that the œstrin excretion has to be examined over a considerable period during the cycle, since occasional analyses are unlikely to provide enough information for an opinion about the nature of the œstrin metabolism. They record the interesting fact that two women whose menstruation was suppressed as a result of coming into hospital for minor operations showed a cycle of œstrin excretion of very much the same type as normally menstruating subjects. Such an apparent contradiction of laboratory and clinical observation must provoke critical consideration of the value of œstrin assays.

A REVIEW OF PUBLISHED OBSERVATIONS

For several years much has been hoped from assays of urinary œstrin as an aid to the diagnosis of certain menstrual disorders and pathological conditions in non-pregnant women. Whether these hopes are likely to be justified can best be judged by comparing the various results of urine analysis in the normal menstrual cycle, which must serve as the common standard of comparison. Much work has been done with the purely scientific object of seeing whether clues to the changes in endocrine activity during the menstrual cycle can be obtained from the changes in the level of excretion of active substances; other work has aimed directly at diagnosing the cause of abnormalities by determining the deviations from an arbitrary normal type of excretory cycle. Unfortunately, when all this work is reviewed, it does not seem that available methods of extraction and assay of œstrin are yet sufficiently standardised or even dependable for any general agreement about the normal levels of excretion and the limits of normal variability.

As long ago as 1926 Loewe and Lange [2] reported that they found œstrin regularly in the urine of the normal woman, and in larger quantities in the middle of the menstrual cycle. Two other investigations [3] indicated the excretion of larger quantities during menstruation, but the existence of this type of variation is not generally accepted. From the work of Siebke [4] in Germany, and of Pedersen-Bjergaard [5] in Denmark, and Frank and his colleagues,[6] Gustavson and Green,[7] Smith and Smith,[8] Gallagher et al.,[9] Yerby,[10] Palmer,[11] Smith, Smith, and Pincus,[12] and Gustavson et al.[13] in America, it seems that the larger body of evidence is in favour of an œstrin excretion curve with two maxima in the course of the menstrual cycle, the first just before the middle of the cycle—which may be correlated with the rupture of the follicle (cf. Séguy and Simonnet [14])—and the second just before menstruation. To discern this measure of agreement is the most one can do: opinion differs as to the relative intensity of these two maxima; as to their absolute values in terms of units of œstrogenic activity, there is a complete lack of agreement which makes it obvious that even in the last two years the assay of urinary œstrin has not reached the simple criterion of reproducibility by different workers.

From the chemical standpoint it may be remarked that attention has rarely been directed to details in the technique of extraction which have been found important with pregnancy urine. The outstanding objection to early work is the failure to set free all the œstrogenic material by adequate hydrolysis, or even to make an adequate separation of the "free" œstrin. In some cases it may be suspected that partial hydrolysis occurred, but in others this cannot be assumed. It appears that, as in many empirical methods of analysis, the adoption of a uniform technique in the hands of a single worker has given results consistent among themselves but lacking absolute value. Again, the methods of biological assay must often be criticised as inaccurate on the grounds that too few animals have been used to give a result correct to within anything like the limits claimed or tacitly assumed by the authors. Further, the general custom of expressing activities not in terms of the international standard substances, but in mouse or rat units—with the underlying fallacy that the mice or rats are international standard objects—makes it extremely difficult to compare the work from different laboratories on a quantitative basis, however possible it may be to discern a general trend of qualitative agreement. A final point which has not been touched by any of this work, with the exception of one paper, is that of the nature of the œstrogens present; how far are the routine methods of bioassay, based on œstrone estimation, applicable to mixtures of several œstrogens whose chemical constitution is a matter of surmise?

The most ambitious investigation of the urinary level of œstrin during a menstrual cycle is that of Smith, Smith, and Pincus.[12]

They compared two methods of extraction of total œstrogens after hydrolysis, one of them including the separation of "œstriol" and "œstrone" fractions—i.e., strong and weak phenols. In general shape their curve agrees with the greater part of the evidence hitherto obtained; there is a high peak of excretion between the 9th and 11th days, a fall, and a broad maximum from the 15th to the 23rd day. In quantity, however, their findings are far higher than any previously reported, the maximum in one day being about 250 "rat units" total œstrin, subdivided into 170 "rat units" (about 65 γ) of "œstrone" and 75 "rat units" (about 30 γ) of "œstriol," the total excretion during the cycle being the equivalent in biological activity of 0·99 mg. of œstrone and 0·46 mg. of œstriol.

[1] Spurrell, W. H., and Ucko, H., *Guy's Hosp. Rep.* 1938, **88**, 230.
[2] Loewe, S., and Lange, F., *Klin. Wschr.* 1926, **5**, 1038.
[3] Laqueur, E., Dingemanse, E., Hart, P. C., and de Jongh, S. E., *Ibid*, 1927, **6**, 1859; Wildebush, F. F., and McClendon, J. F., *Proc. Soc. exp. Biol., N.Y.* 1929, **26**, 785.
[4] Siebke, H., *Zbl. Gynäk.* 1929, **53**, 2450; 1930, **54**, 1601, 1734; *Arch. Gynaek.* 1934, **156**, 317.
[5] Pedersen-Bjergaard, K., *Zbl. Gynäk.* 1936, **60**, 372.
[6] Frank, R. T., *J. Amer. med. Ass.* 1931, **97**, 1852; Goldberger, M. A., and Spielman, F., *Ibid*, 1934, **103**, 393.
[7] Gustavson, R. G., and Green, D. F., *J. biol. Chem.* 1934, **105**, xxxiv.
[8] Smith, G. Van S., and Smith, O. W., *Amer. J. Physiol.* 1935, **112**, 340.
[9] Gallagher, T. F., Peterson, D. H., Dorfman, R. I., Kenyon, A. T., and Koch, F. C., *J. clin. Invest.* 1937, **16**, 685.
[10] Yerby, L. D., *Proc. Soc. exp. Biol., N.Y.* 1937, **36**, 496.
[11] Palmer, A., *Ibid*, 1937, **37**, 273.
[12] Smith, Smith, and Pincus, G., *Amer. J. Physiol.* 1938, **121**, 98.
[13] Gustavson, Hays, E. E., and Wood, T. R., *J. biol. Chem.* 1937, **119**, xlii; Gustavson, Mason, L. W., Hays, Wood, and D'Amour, F. E., *Amer. J. Obstet. Gynec.* 1938, **35**, 115.
[14] Séguy, J., and Simonnet, H., *Gynéc. et Obstét.* 1933, **28**, 657.

The ratios of the excretion of "œstrone" to "œstriol" are regarded by them as in keeping with the assumption [13] that œstradiol is converted, when the ovaries are present, into œstrone, and that the latter, in the presence of progestin, is converted into œstriol. The "œstrone"-"œstriol" ratio was twice as high during the first two days as at any other time. More "œstrone" than "œstriol" was present throughout. More "œstriol" was excreted during the luteal phase than during menstruation and the period of follicle ripening. A rise in "œstrone" accompanied menstruation.

Confirmation and extension of this work will be awaited with interest. A striking feature of it is the high yield of œstrogen claimed in the single case examined in detail. At this level there would be some hope that chemical and colorimetric methods of assay might be developed and replace the laborious biological assay.

NEED FOR CAUTION

It is unfair to complain when a research, whose object was investigation of a fundamental physiological problem, is not immediately applicable to clinical practice. One must, however, admit the necessity of the precaution, insisted on by Frank et al.,[6] of examination throughout a whole month to determine the type of abnormality of one patient, and it is obvious that an examination entailing assays with hundreds of animals on 24-hour urine specimens collected over a month is impracticable as an ordinary diagnostic aid in menstrual disorders. Yet the one cycle of the one patient examined by Smith, Smith, and Pincus cannot be taken as a yardstick by which others can be judged. Gustavson et al.[13] found that in three women, all gynæcologically normal, individual variation was very large, as regards both the magnitude and the time of the maxima of œstrogen excretion.

The cautious attitude of Spurrell and Ucko commands attention and evidently an assay of urinary œstrin on a single specimen cannot be of any diagnostic value except in extreme cases of excessive œstrin secretion. Examination of conditions during the normal menstrual cycle is still in the research stage, and the conditions in menstrual disturbance still await proper exploration.

AUSTRALASIA

(FROM OUR OWN CORRESPONDENTS)

NUTRITIONAL SURVEY OF THE INLAND

WORKING under the auspices of the Commonwealth Advisory Council on Nutrition, Dr. F. W. Clements of Sydney has conducted a comprehensive nutritional survey of the remote regions of the interior of South Australia and of the three eastern States. Out of a total of 3384 children examined, 607 (or 17·9 per cent.) showed evidence of unsatisfactory nutrition. The figures varied from 23·7 per cent. in western New South Wales to 13·3 per cent. in the Victorian mallee. All school-children were examined, together with a high proportion of pre-school children, and a number of children living considerable distances from school, who receive their education by correspondence. A physical and clinical examination determined whether the state of nutritional development of the child was "satisfactory" or "unsatisfactory." Those children falling into the latter class and a number of the "satisfactory" type were submitted to an X ray examination of the epiphysis at the wrist, a hæmoglobin estimation, Göthlin's capillary resistance test for scurvy and border-line scurvy, and a visual acuity test for partial night-blindness. By the application of these methods it was possible to select cases of malnourishment, and, in the majority, to detect the effects of the malnutrition.

No scurvy was found, but rickets affected from 6 to 11 per cent. and nutritional anæmia from 4 to 6 per cent. of the children examined. The rickets figure was higher in the smaller and more remote settlements, and the most evident signs were found in infants 12–24 months of age. Dr. Clements considers that insufficient phosphate intake is the greatest factor involved in the high incidence of rickets. Sunshine is abundant in the inland areas, and drinking water is rich in lime. The scarcity of milk in the interior is an important cause of the deficiency. Undernourished children, free from rickets but underweight, pale and thin, were found to be on a high carbohydrate diet, with excess of lollies, cakes, and biscuits, and a low fat intake. An attempt was made to relate the diets of the children to their nutritional state. A rough investigation showed that while 6 per cent. of those children whose diets were judged to be satisfactory were suffering from malnutrition, the figure was 63 per cent. among those whose diets were considered inadequate and generally unsatisfactory. A further series of these examinations is being carried out by Dr. Clements among pre-school children at baby centres in Sydney. In this way, using the methods and technique of the inland survey, it is hoped to correlate the findings in city and country children.

SLEEPING OUT

The latest census for the Commonwealth shows that 4·5 per cent. of the occupants of private houses and 3·8 per cent. of the occupants of flats regularly sleep out on unenclosed verandahs. In the provincial areas 5·3 per cent., in the rural areas 5·0 per cent., and in the metropolitan areas 3·7 per cent. of the population sleep outside. These figures do not include those occupying permanently enclosed outdoor sleeping places, who are regarded for census purposes as inmates of rooms. As anticipated, owing to climatic conditions, the largest number sleeping out on unenclosed verandahs was recorded in Queensland, 7·6 per cent.; followed by Western Australia 7·0 per cent., New South Wales 4·9 per cent., Victoria 2·7 per cent., South Australia 2·5 per cent., and Tasmania 1·8 per cent.

THE HEALTH OF NEW SOUTH WALES

The annual report of the director-general of public health for New South Wales shows that the infant mortality for 1936 was 43·47 per 1000 live births—a figure 3·62 higher than the average of the previous five years. Of the specified causes of death the rise is principally among the group classified as "prematurity," over a third being certified as due to this cause. Attention is drawn to the difficulty of inducing expectant mothers to avail themselves of the facilities at antenatal clinics. Attendances at these clinics were fewer in 1936 than in 1935. The maternal death-rate (5·1 per 1000 live births) was the same as that for 1935, and shows little tendency to fall, in spite of organised efforts to reduce it. Of the infectious diseases, diphtheria was unusually prevalent particularly during the first half of the year. The figures show that although the incidence is much lighter under five years of age, the death-rate is considerably heavier. From May onwards there was

[13] Pincus and Zahl, P. A., *J. gen. Physiol.* 1937, **20**, 879.

an active campaign for immunisation throughout the State, and on the whole there was a good response. At the end of 1936 43,300 children (in a total population of 2,700,000) had been immunised. Inquiries made into the after-histories of tuberculous patients admitted to sanatoria in 1931 disclosed that 50·7 per cent. had died. Until recently the tuberculosis division of the department of health has had to treat only those persons who had little prospect of recovery. Recently the department has been concentrating on a search for early cases known or suspected to have been exposed to infection.

Notified cases of venereal disease show a slight increase over those for the previous year, but there has been a decrease in the number of persons reporting with a primary syphilitic infection. During the year prophylaxis was used by 999 persons, only a fifth of whom had associated with a prostitute before seeking protection. It is also pointed out in the report that infection is often a result of carelessness and laziness. Of the 280 former patients who returned to the clinic with fresh infections, all knew of the prophylactic facilities available, but none had attempted to protect themselves.

UNITED STATES OF AMERICA

(FROM OUR OWN CORRESPONDENTS)

A FRESH ATTACK ON TUBERCULOSIS

"A London Practitioner"[1] remarks that "every 'campaign' against a major disease . . . brings with it its wave of fear"; and the same criticism is sometimes made by those in private practice in this country. He goes on to say, however, that "perhaps these people would be afraid anyway," and he includes a case of anxiety neurosis among the first dozen patients in his day-book for 1938. So he also contributes the answer to his own criticism.

Public health workers who start these campaigns are doubtless influenced by the great administrative advances that resulted from fearful catastrophies like the pandemic of cholera in 1832. Yet they would have to admit that fear of contagion was but one of the social forces responsible for the development of public health in Britain. As Simon showed,[2] the rise of humanitarianism in the century 1738–1838 provided an indispensable condition for the success of Chadwick's report in 1842, and in the writings of Chadwick and of Southwood Smith may also be found a very plain appeal to economic self-interest. It is interesting to trace these same forces in the campaigns developing in this country against syphilis, poliomyelitis, rheumatism, and (now with suddenly renewed vigour) tuberculosis.

The paper delivered by the late Wade Hampton Frost[3] a year ago has had a big influence and deserves close study. He urged that as tuberculosis cases become fewer and fewer preventive measures should be centred more and more upon the open cases; that the protection afforded to contacts should be progressively increased; and that wherever the contacts are exposed to the double menace of infection and poverty, protection against both should be afforded. Already New York State has set itself the goal of isolating all infectious cases for the duration of their infectiousness, wherever contact is dangerous to others, and we no longer hear of "early" cases being preferred for sanatorium care. In other parts of the country the provision of sanatorium beds is inadequate for the inauguration of such a policy, and the building of new institutions for the treatment of a disease that is rapidly declining in importance may seem like an extravagance. Nevertheless, Bailey B. Burritt, general director of the New York Association for Improving the Condition of the Poor, has presented estimates that make such expenditure appear very desirable from the viewpoint of economic self-interest alone. Using the estimates of Dublin and Lotka on the economic value of human beings, he finds the asset value of the present tuberculous population to be $4,000,000,000; and assuming that these patients retain on the average one-third of their working capacity the loss through tuberculosis becomes $2,600,000,000. He contends that there is at least a sufficient basis of reliability in this estimate to conclude that enormous values are needlessly lost in this country.

To prevent this loss Mr. Homer Folkes, executive secretary of the New York State Charities Aid Association, has prepared a six-year programme of Federal and State expenditure. This was made public on June 20th after it had been endorsed by the board of directors of the National Tuberculosis Association and by Thomas Parran, surgeon-general of the U.S. Public Health Service. The estimated total cost of the programme is $269,044,000, of which the Federal Government will be asked to provide $176,522,000. The distribution of these funds is as follows: hospital construction, $140,000,000; hospital maintenance, $113,000,000; and case-finding, $15,544,000. The Federal Government will, it is hoped, bear about 80 per cent. of the cost of hospital construction and half the cost of hospital maintenance and the ascertainment of cases. The programme provides for 40,000 additional beds at an estimated cost of $3500 per bed, and maintenance is calculated at $750 per patient per year. The cost of X ray examination is set at $7—a figure that seems unnecessarily high in view of the large scale on which this programme is planned. It is recommended that "since the States differ very widely in the nature and extent of antituberculosis provisions . . . no one fixed plan of Federal State coöperation should be laid down. The programme should be frankly opportunistic." This is sound advice. It remains to be seen whether Congress will find it acceptable.

[1] Grains and Scruples, *Lancet*, 1938, **1**, 1415.
[2] Simon, J., English Sanitary Institutions, London, 1890.
[3] How Much Control of Tuberculosis? *Amer. J. publ. Hlth*, 1937, **27**, 759.

BUCHAREST

(FROM OUR OWN CORRESPONDENT)

DEATH OF QUEEN MARIE

MOST of the medical societies of Rumania sent delegates to the funeral of Queen Marie and the General Medical Association sent a telegram to King Carol expressing the sense of loss felt by the profession at the death of one who played so large a part in the creation of the present Great Rumania.

AMMONIUM THIOCYANATE POISONING

The use of potassium rhodanate (thiocyanate) in chronic arthritis, advocated in a French medical journal in 1932, led Prof. Orient to give it a trial in a woman of 50 suffering from chronic articular rheumatism. He prescribed 50 drops a day of a 25 per cent. solution, but after his patient had used two bottles of the mixture she got intense dryness, pain, and swelling of the mouth. Her pupils were widely dilated, and did not react to light, and her pulse

and respiration rates were very fast. Atropine poisoning was suspected but it was later found that the chemist had dispensed ammonium rhodanate for the potassium salt. The patient was forthwith given two injections of pilocarpine and recovered in ten days.

"THE CITADEL" IN RUMANIA

Cronin's novel "The Citadel," which was published in Hungarian and was very popular in Transylvania where the Magyars bought it with great eagerness, has been banned by the Rumanian authorities. The book had also been published in a Rumanian translation which was just as popular. The enactment, prohibiting the sale of the book in any translation or in English, states that it may shake the belief of the patient in his doctor, all the more so as the present generation is so prone to scepticism. Those who have been ill know that it is not only medicine that cures but also faith and trust in the doctor. The Rumanian press, commenting on the ban, says that it is very desirable. The book had an unprecedented sale and in the circulating libraries it was weeks before one could borrow it. In these days, writes a leading medical journal, the task of the doctor is more difficult than it ever was. Therefore, only those books should be given to the public which do not impede but help the doctor in his work. Cronin's book did not help. It had to be banned not in the doctors' interests but in the interests of sick people. It is not doubted that patients who are ill, even if they do read Cronin's book, will nevertheless consult a doctor; but if they do call a doctor they should have a firm belief that he will relieve their pains and cure their diseases.

PARIS

(FROM OUR OWN CORRESPONDENT)

CRIMINAL ABORTIONS

IN a communication to the Academy of Medicine Dr. J. Okinczyc and Dr. P. Denoix make some shrewd comments on their hospital experience of criminal abortion. In their surgical service for women they found in 1937 that the largest single group of ailments was that representing the sequels of induced abortion, which accounted for about a sixth of all their cases. The growing frequency with which such sequels bring women to hospital is, in their opinion, real, not merely the result of a growing tendency to prefer treatment at hospital to treatment at home. Of 242 cases 3 were fatal, but it was observed that little attention had been paid to the warning of disease and death as sequels to induced abortion. Apparently such warnings are commonly regarded merely as attempts by doctors to keep the pregnant woman from moral error. The warning which she heeds more attentively is that sterility may be a consequence. This prospect does not merely conjure up a vague picture of biological inferiority; it warns the far-seeing woman that at some later date the possession or prospective possession of a child may be a valuable pawn in the game she plays with a potentially faithless husband.

MEDICAL SUPERVISION OF UNIVERSITY STUDENTS

In June the President of the Republic signed a decree the opening sentence of which runs as follows: "The universities are authorised to institute a service of medical control and mutual aid on behalf of students." This decree links up in a comprehensive scheme the sporadic efforts of certain French universities to take care of the bodily welfare as well as the intellectual development of their students. Strasbourg has been a pioneer in this field, having even before the late war provided a system of sickness insurance for its students. In 1929 this system was converted into a veritable centre of preventive medicine. The University of Nancy followed suit in 1932, and the examples thus set by these two provincial universities have in turn been followed by those of Paris, Bordeaux, and many others. At the University of Grenoble, for example, as high a proportion as 77 per cent. of the students recently matriculated have spontaneously joined in the working of such a scheme. At other universities it has languished for want of the necessary driving force in certain quarters. Hence the decision to infuse uniformity and prestige into the scheme by a Presidential decree. The Union Nationale des Étudiants de France has recently passed a unanimous vote in favour of a unified system applicable to all the universities, and the same body has agreed to the principle of a contributory scheme, with a fee of 50 francs from each student. In a memorandum on this subject addressed to the President of the Republic by the Prime Minister and the ministers of education, health, and finance, it is pointed out that it behoves the country without delay to set this scheme in operation, and in this respect to make France as well equipped as any of her neighbours.

MEDICINE AND THE LAW

Prison or Hospital for Drug Addict?

LAST week the Marylebone police-court magistrate sent a 22-year-old girl to prison for four months in the second division in the hope of permanently curing her addiction to drugs. She had pleaded guilty to four charges of obtaining, or attempting to obtain, Omnopon. She admitted 22 other cases of obtaining the drug from chemists by means of forged prescriptions. While the accused was under remand there had been suggestions of an arrangement for her treatment in a London hospital. These apparently broke down. After he had passed sentence, the magistrate was asked by the defence to consider an alternative proposal of institutional treatment. A doctor was present in court who was prepared to give information of arrangements made for the defendant to enter a hospital for nervous diseases and remain under his personal care. The magistrate refused to alter the decision which he had already given. He had previously remarked that experience showed the grave temptation of patients undergoing voluntary treatment during the period when the quantity of the dose was being reduced. There was nothing to prevent the patient from walking out and procuring a fresh supply, thus spoiling the effect of the treatment. In prison, on the other hand, doctors could exercise a proper control in the interests of the patient without the risk of interruption.

The magistrate imposed the sentence of four months after hearing medical evidence that the period likely to be necessary for treatment was from two to three months. Without the slightest desire to suggest that in this case (in which notice of appeal has been given) or in any cases of a similar kind a long term of imprisonment would be proper, it will be recalled that, twelve years ago, the departmental committee on morphine and heroin

addiction was much less optimistic as to the time needed for a cure. Its report mentioned that several witnesses had pressed upon the committee the view that the actual reduction of doses down to the final point of total withdrawal of the drug was only the first stage in treatment, if a complete and lasting cure was to be looked for. It was said that permanent cure could not be claimed unless and until the addict had remained free from his craving for a period variously estimated as from 1½ to 3 years after the final withdrawal of the drug. Nor was the committee able to furnish any solid statistics of the proportion of cases in which permanent cure was established. The patient's physical condition must be restored and will-power fortified. The prison doctor has an enviable power of control in the early stages of treatment. In the therapy of drug addiction as in that of mental instability voluntaryism is at a disadvantage. Hospital staffs are not warders and wardresses; their best efforts may be wasted if the patient, lacking the will to return to normal health, walks out. Many a doctor has patients of all kinds whom he could quickly cure if he could treat them within a prison wall.

CORRESPONDENCE

SPINAL ANÆSTHESIA

To the Editor of THE LANCET

SIR,—I should like to express my appreciation of Mr. Norman Lake's paper in your issue of July 30th on precision in spinal anæsthesia, and from personal experience to endorse his account of the excellent results obtainable by the use of reduced doses of 1 : 1500 Percaine.

For the past four years, while working for Mr. Kenneth Parsons at Dudley-road Hospital, Birmingham, I have been using a spinal anæsthetic technique for 1 : 1500 percaine similar in principle to that described, and in 340 cases it has not been necessary to exceed a maximum dose of 10 c.cm.—the minimum dose used being 5 c.cm. In this technique, which I described in March, 1936, at a meeting of the anæsthetics section of the Royal Society of Medicine, the spinal injection is given with the patient in the lateral position, after which he is turned on to his face and the level of anæsthesia is controlled simply by tilting the whole table in an "anti-Trendelenburg" direction and lowering the head-piece so that the highest point of the spine is over the joint of the table. When a high anæsthetic is required, the patient is arranged on the table so that the first dorsal spine is the highest point and in this case a full "anti-Trendelenburg" tilt is required. When a lower anæsthetic is required, the position of the patient and the tilt of the table are modified. Three minutes in this position is sufficient to produce the required height of anæsthesia, after which the table is levelled and the patient turned on to his back so that preparations for the commencement of the operation may be carried out.

We have found this method entirely satisfactory for all sizes and shapes of patients and one can produce very satisfactorily controlled spinal anæsthesia by its use. In addition to the usual dose of ephedrine, all patients are premedicated with hyoscine followed by hyoscine and morphia so that the majority are entirely oblivious of the whole proceedings and are unaware that they have left the ward at all.

I am sure that Mr. Lake's emphasis on the necessity for slow injection of the solution is of the greatest importance. At one time I used to inject more rapidly and for high spinals used to make my puncture between dorsal 12 and lumbar 1, but since increasing the injection time to two minutes I have never needed to puncture higher than the orthodox 2nd lumbar space.

With regard to the after-treatment, we have not found it advantageous to maintain a head-down position for any length of time. All cases which are normally nursed in the Fowler position are placed in this position eight hours after operation. The patient is kept flat for one or two hours after which he is raised slowly, one pillow being added at a time until the required position is reached. I am sure that this practice is a very important factor in the prevention of chest complications, which have been reduced to the minimum.

The number of patients who have developed spinal headaches averages less than 2 per cent. and there have not been any other neurological sequelæ in the series. I am, Sir, yours faithfully,

MARGARET GALBRAITH.

Birmingham, August 12th.

MATERNAL MORTALITY AND MEDICAL EDUCATION

To the Editor of THE LANCET

SIR,—The letters of Sir E. Graham-Little and Dr. Falla have made me realise that one further comment on Dr. Summerskill's recent diatribe is desirable. Having qualified in the same year and from the same medical school as Dr. Summerskill, in common fairness to that school I want to make it clear that her unfortunate experience was unique. A medical school that enjoyed the honour of having Eden, Lockyer, and the late Bright Banister successively in charge of its obstetric teaching has every reason to be proud of the record; and we who learnt our obstetrics in that school have ourselves alone to blame if we (or any one of us) were foolish enough not to make full use of the opportunities provided for the gaining of experience in practical midwifery.

I am, Sir, yours faithfully,

M. SCOTT.

Capel-road, East Barnet, August 14th.

To the Editor of THE LANCET

SIR,—I find Sir Ernest Graham-Little's letter somewhat difficult to understand. If he is making an appeal on behalf of a most excellent maternity hospital he will have the sympathy and support of everyone; but if he is attacking a woman M.P. who is doing her best to remedy a discreditable situation he is likely to meet some opposition. Dr. Summerskill was stressing the need for better midwifery and is supported in her plea by the compilers of the 1937 Maternal Mortality Report, who tell us that "maternal mortality is too high, is capable of reduction," and that "inexpert midwifery is a factor of major importance." At a recent medical meeting a professor of obstetrics said that local authorities could have in large measure that reduction in maternal mortality for which they were prepared to pay, and this statement is well borne out by the recently published results of L.C.C. hospitals. Among the booked cases at these hospitals the mortality was under 2 per 1000, so that the present figures published by the Ministry of Health, giving the national

maternal mortality as over 3 per 1000, are no cause for congratulation or complacency.

I would entreat Sir Ernest and other elder statesmen to realise that all is not for the best in the best possible of worlds, and to have more patience with those of the younger generation who are at least making some personal effort to leave this world a little better than they found it. Sir Ernest and his friends have been given every opportunity over a great number of years to provide a satisfactory national maternity service. They have not done so and it was not until there was a public outcry that any active steps were taken.

I am, Sir, yours faithfully,

J. E. ELAM.

Station-road, New Barnet, August 12th.

OXYGEN INJECTION FOR SCIATICA

To the Editor of THE LANCET

SIR,—The treatment of sciatica by injection of oxygen into the subcutaneous tissue of the thigh is painless, and in many cases extraordinarily effective, yet it seems to be very seldom practised. Dr. J. P. Martin in 1927 wrote: "This method of treatment is suitable for acute and subacute cases, and though it may be somewhat uncertain, its extreme simplicity makes it always worth trying . . . two or three injections often give the most surprising relief."[1] Dr. James Collier and Dr. W. J. Adie gave similar advice: "Massive injections of oxygen into the region of the affected nerve, is a simple and harmless process, which gives no pain, and often brings most conspicuous relief."[2] It is surprising, therefore, to find that at the recent discussion on sciatica at Plymouth, Dr. Wilfred Harris,[3] referring to the remedies available, such as drugs, heat, massive and epidural injections, weight extension, and even the application of a plaster, made no reference to this simple and effective method; neither was it mentioned by any of the other speakers. Yet there can be no doubt that in cases of sciatica attributed to interstitial fibrositis of the nerve, the massive injection of oxygen into the subcutaneous tissue may produce an almost miraculous effect, and it is equally successful either in the early or the late stages of the disease. My personal experience of the treatment is comparatively small, but in the cases I have seen the effect has been very striking.

A man who had been completely incapacitated by sciatica and confined to bed for several months obtained little relief from any previous treatment, with the exception of saline injections into the nerve, but after injection of oxygen he was able to walk without pain and returned to work.

In another case, a member of my own family had been incapacitated for about five months, and treatment, including epidural sacral injections (which were very painful), gave little if any relief, but two or three injections of oxygen brought a speedy cure. The neuritis was apparently caused by absorption of streptococcal toxin from a chronic tonsillar focus.

The treatment is equally efficacious at an early stage of the disease, as in the case of a woman who had been only a week in bed with sciatica and was completely relieved after three injections.

The method of use is to have a cylinder of oxygen with fine adjustment tap connected by rubber tubing, via a wash-bottle containing warm water, with a sterile Record needle about 1 mm. in diameter and 2½ in. in length. The oxygen is allowed to bubble gently through the water and the needle is introduced an inch or more into the middle of the back of the thigh just below the gluteal fold. The gas infiltrates the tissues until the whole of the back of the thigh and gluteal region are "ballooned up," when the needle is removed. The subcutaneous emphysema subsides during the next 48 hours when the process may be repeated lower down the thigh over the line of the nerve.

No pain is complained of, although there may be a feeling of tension of the skin for a short time. Two or three injections often result in complete cure. It seems probable that the same method would be equally effective in the treatment of brachial neuritis—e.g., of the musculospiral nerve.

I am, Sir, yours faithfully,

HERBERT H. BROWN.

Worthing, August 2nd.

[1] Martin, J. P., Modern Technique in Treatment, vol. iii, London, 1927, p. 100.
[2] Collier, J., and Adie, W. J., in Price's Textbook of the Practice of Medicine, London, 3rd ed., p. 1656.
[3] *Lancet*, July 30th, 1938, p. 260.

THE EMERGENCY BED SERVICE

To the Editor of THE LANCET

SIR,—Recently I was called to a case of food poisoning. A mother and her child of 3 years had collapsed, and in addition there was a 2-month-old baby with no one to look after it. I felt that the mother and child urgently needed hospital treatment. I rang up the emergency bed service of King Edward's Hospital Fund for London. Within fifteen minutes they had found suitable hospital accommodation for the sick mother and child and also the baby (which was not affected).

I cannot express my thanks for this excellent new service. I had fully anticipated an hour's telephoning to get these cases into hospital. I fancy that if only other practitioners realised the excellence of the organisation it would be much more widely used.

I am, Sir, yours faithfully,

P. G. S. KENNEDY.

Balaam-street, London, E.

MEDICAL HELP FOR SPAIN

To the Editor of THE LANCET

SIR,—Recent reports from Spain tell us of the magnificent way in which a modern hospital system is being evolved out of the emergency and improvised medical services of the earlier war days. We are very proud of England's share in this, for the Spanish people acknowledge with deepest gratitude and appreciation our nurses and doctors, our instruments and equipment, our ambulances and supplies.

Unfortunately, we can never send enough. The needs grow with each air raid, with every offensive. Here are two quotations from letters just received from a member of the Spanish Medical Aid Committee in Barcelona:—

". . . You remember Dr. . . . with whom we have had nurses working since the first days at Grañen. He has now been at the front for 20 months and has been recalled to his own civil hospital in Barcelona. He is one of the finest surgeons in Spain, so you can imagine his horror when he discovered that there was absolutely nothing in the operating theatre with which to do surgical work, although the results of bombardments were filling his wards. I have seen the theatre myself—there are 19 surgical instruments only, and every one is broken. A little boy was brought in while I was in the hospital with a scalp injury and fractured skull. They could do nothing for him as they had not the proper instruments—and so he just died. I am sending a list of the most urgent necessities. . . . If they could have those, it would help them

along and perhaps later when you have more money we could do something for them. . . ."

These elementary necessities cost £111. They were bought and sent out on Tuesday last.

". . . An X ray apparatus is very badly needed for the blood-transfusion service here. . . . There can be little doubt that at the moment, this is the most urgent necessity in Spain on the medical side. We ought to be very proud of the assistance we have already rendered to this service. On the day of my arrival blood was being rushed up to the front in the two vehicles we have given to them, and without which it would have been impossible to get out the supplies of blood necessary for the big offensive. Dr. Duran has twice devoted some hours of his time to showing me the complete organisation for this great work and I have seen the blood being taken from the donors. On the night before the offensive began a radio message was sent out asking for donors. The next morning there was such a response that it was difficult to push one's way into the building. They have now 14,000 donors on their lists, and all day and every day they have at least 200 contributing blood. On such a day as I have mentioned, many more. These donors give their blood once a month, so you can gather something of the size of the organisation. But now a very tragic difficulty has arisen. Due to malnutrition, a large number of people in Barcelona and Eastern Spain are tuberculous. It is absolutely necessary, as the doctors on the Committee will realise, to make sure that blood is not taken from these people. In order to avoid this, an X ray apparatus for screening chests is an immediate necessity. . . ."

This will cost £320, and we cannot supply it as we have not the money.

May we appeal for contributions to enable us to meet this need? It would be a splendid gesture if this X ray apparatus could go out from the medical profession here to assist their colleagues in Spain. Cheques may be sent to the treasurers, Spanish Medical Aid Committee, 24, New Oxford-street, London, W.C.1, letters being marked "X ray."

I am, Sir, yours faithfully,

H. JOULES,
On behalf of the Spanish Medical Aid Committee.

August 12th.

A COMMITTEE ON BLINDNESS

To the Editor of THE LANCET

SIR,—Under the heading "Medical News" on p. 404 of your last issue there is a note as to the constitution of the Advisory Committee on Blindness appointed by the Minister of Health. Of the thirteen members, ten belong to the medical profession. Considering the important rôle played by syphilis and gonorrhœa in the causation of ocular damage, the committee would, I suggest, be strengthened by the addition of a venereologist. At the same time, those who are superstitious would feel that any "hoodoo" attaching to the ill-omened number 13 would thereby be removed.

I am, Sir, yours faithfully,

E. T. BURKE.

Elm Park-gardens, S.W., August 13th.

GRAINS AND SCRUPLES

Under this heading appear week by week the unfettered thoughts of doctors in various occupations. Each contributor is responsible for the section for a month; his name can be seen later in the half-yearly index

BY ANOTHER READER

III

Aldous Huxley used to think that the world in general had no meaning at all—"meaning" here being a "spiritual" value—and therefore he could amuse himself as he pleased in it. Looking back he now thinks that his desire for amusement was primary and his belief in the world's meaninglessness was a justifying rationalisation. He now grants "meaning" to the world and from that argues that it should be possible to improve the unhappy state in which human society, Science aiding it, has landed itself; the attempt at reform, which before was merely superstitious, now becomes worth while. So Huxley turns reformer, and examines at length the *Ends and Means* of social and international betterment. He takes the ends to be—by common consent of the best of mankind—"liberty, peace, justice, and brotherly love." He has no glib formula for achieving those ends, but in what he calls a cookery book of reform he suggests many ways in which we might move some distance in their direction. He eschews all violent and cruel means, such as revolutions, on the ground that their toxic side-effects more than counterbalance their therapeutic benefit, and he is greatly interested in reshaping the machine-like structure of large-scale organisations into some more human form. He wants to supersede "mechanomorphism" both as a philosophy and as a way of living.

* * *

Whether the true origins of the reformer's zeal lie, after this fashion, in his philosophy of life, I hardly know. It may be that the two things just go together in some obscure way, like mind and body. Among doctors in general I think that both real keenness on reform and a professedly idealistic philosophy are uncommon. Most of us look on human nature as "always the same"; it is one of the things you can't change. We find it interesting and take some pride in the special opportunities our profession gives us of observing it, but we feel little urge to try to improve it, especially in its social behaviour. Or we find ourselves so much occupied with improving its bodily habitat that we look on its morals as someone else's job. So far as our handling of the individual patient is concerned, that attitude is becoming more difficult to maintain since the development of medical psychology and the recent emphasis on "seeing the patient as a whole." If it is obscurantist (in the words of Lord Horder's Conway lecture) to separate the health of the body from that of the mind, or the health problems of manual workers from their economic conditions, then we as doctors must concern ourselves with our patients' loves and hates, their greeds and their unselfishnesses, and their relations with the community in which they live. In these matters, moreover, we have to believe that there exists a possibility of improvement, of progress; that at least must be our working hypothesis—otherwise how can we work? The medicine of the body would be a futile art without the *vis medicatrix naturæ*, and this wider medicine of the whole man is humbug if we hold that human nature is immutable. It may even require, as a growing number of psychotherapists are coming to believe (see *Lancet*, August 6th, p. 325), that the medical man should adopt a positive religious

outlook. The wider view is right, I feel sure, though I confess that its implications for the practitioner of the art of medicine are overwhelming. Time was when the family doctor's official business was to look after his patients' bodily ailments; incidentally he helped them, when opportunity offered, so far as his wisdom, experience, and personality allowed, in their problems of conduct and living. But now is he to set himself up officially as a healer also of the mind and a guide in morals? We can scarcely imagine that adding a course in psychology to the curriculum will equip him for the composite task of doctor, pastor, and general welfare-worker. The task is too big, yet at least, for medicine to claim entirely for itself, but medicine with or without outside coöperation must make some attempt at it; which means that doctors are obliged by the logic of their profession to be in some degree private and public reformers.

* * *

I am far from suggesting that the Royal Society of Medicine should have a section that meets in Hyde Park on Sundays, or that the College of Physicians—that august body in search of new functions—should run a revival campaign throughout the country. Medicine has no use for the methods of mass propaganda, for in patients it has learned to respect people as individuals. Nor do I welcome the over-zealous reformer, who calls out, either pathetically or violently, for the sudden creation of his new Jerusalem to-morrow. But I could wish that more of us had just a dash of the reforming spirit in us. In the way in which our work for the community is organised, for example, we might be more ready to admit that it could be improved, and could go on being improved; we should be more willing to experiment now and then with new ideas. There is plenty of that spirit in the practice of medicine, where half of therapeutics is a matter of trial and error, critical or uncritical, but there is little of it in the attitude of the profession to the organisation of practice. Changes are taking place, it is true, but nearly always from the external pressure of the community on the profession, and nearly always in the direction of making the doctor a salaried servant of a large autocratic centralised authority. Except for some development of partnership practice, and an occasional private clinic like New Lodge, little constructive change has originated within the profession, which is mostly concerned to defend its traditional economic individualism against the encroachments of outside authority, though the defenders usually admit with a wry face that they are fighting a losing battle. Huxley sees little but evil in the large-scale organisation ruled from above by a hierarchy of little dictators, each handing responsibility up to his superiors and passing down orders and reprimands to those inferior to him. That is the army structure, most efficient for mechanical or military purposes but ill-adapted for any approach towards his ideals of liberty, justice, peace, and charity. It tends rather in the other direction; yet it is the model of most industrial organisation, it is the pattern of some of our new municipal medical services, and it certainly will be the pattern of any State medical service organised by the State. The only hope of avoiding it is that, while there is still time, the profession should abandon its die-hard defence of competitive individualism and devise some sort of truly democratic coöperative structure.

* * *

Huxley's remarks on the number of individuals in a self-governing group may be relevant here. He observes that eight is the perfect number for a dinner-party, that Jesus had twelve disciples, that a communist cell contains ten members, that few committees of more than a dozen people work well; that in general, for intellectual or social purposes, the optimum number for a group lies between five and twenty. Within those limits, the members of the group will be loyal to it, feel personally responsible for its actions, tolerate their colleagues, and share in its government; increase its size and either it will split into sub-groups or the sense of responsibility will go and it will display the lower moral standards and the curious emotional sub-human behaviour of the mob. He quotes a French economist, Dubreuil, who claims that industrial concerns can be successfully organised on the basis of a series of self-governing yet coördinated groups of up to thirty workers. Is this principle applicable in medicine? The nearest existing parallel is the staff of a voluntary hospital, which in most essentials successfully governs itself. The wise reformer tries to develop existing institutions and precedents where they conform to his principles. It should be possible to organise a municipal medical service on democratic lines, giving the staff of each hospital much more independence, more responsibility, more voice for example in the choice of their colleagues than many of them at present enjoy. The wise reformer also sets an example on a small scale before he tries to realise a new idea all over the country. A trial might well be made in one district of organising salaried general practitioners into small groups working in coöperation with their local hospital and really sharing in its government. The whole trend of the present army-like structure is towards centralisation of authority and responsibility, making the units at the periphery into automatons; the hope of liberty and development for the individual—in conditions where some large-scale organisation is unavoidable—lies in decentralisation of authority and responsibility, with arrangement of individuals in groups of appropriate size, each enjoying the maximum of independence and self-government compatible with cohesion of the whole. Ask me to work out the full details of such a scheme here and now, and I take refuge in the architect's excuse who will not draw a plan of his house until he sees the actual site. Nevertheless I feel that on lines like these the medical profession could reform its structure in adaptation to modern social changes and yet retain for its members a fair measure of liberty, justice, and peace, incidentally setting a useful example to the community at large; whereas if we let things drift on as they are going now we shall fight for our cut-throat individualism until we find ourselves cogs in a machine.

*** *This concludes the three articles by Another Reader. Next month A Hakim will be responsible for these columns.*—ED. L.

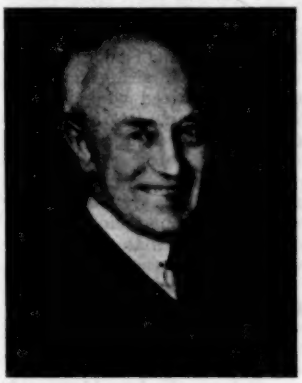
BRITISH PHARMACEUTICAL CONFERENCE.—The seventy-fifth meeting of this conference will be held in Edinburgh from Sept. 12th to 16th. The address at the opening session will be delivered by Mr. J. Rutherford Hill, the chairman of the conference, at 3 P.M. on Sept. 12th, and in the evening there will be a civic reception by the Lord Provost, magistrates, and council of the city. On the evening of the following day there will be a banquet at which the president of the Pharmaceutical Society, Mr. Thomas Guthrie (who is ex-officio president of the conference), will be one of the speakers. Twenty-three papers will be contributed at the science sessions and pharmaceutical politics will be discussed at the meeting of branch representatives. On Sept. 16th there will be an excursion to the Perthshire Highlands.

OBITUARY

ALEXANDER SHEARER, O.B.E., M.B. Glasg.

As briefly announced in our last issue, Dr. Alexander Shearer has died in Edinburgh in his sixty-seventh year. At the Department of Health for Scotland he was the medical officer whose work was devoted to the Highlands and Islands Medical Service, and his unique services for twenty years to the area for which he was responsible were rewarded by an extension of his period of duty for two years beyond the normal time of retirement.

Shearer's life and work were a fine example of the old Scottish tradition in education. He was the eldest of eleven children of a blacksmith in Armadale. His father having moved to Dumbarton, the boy received his early education in the Academy there; and although, as he recalled, he was the only barefoot boy in the school, his brightness as a pupil won for him a bursary. His mother, with the shy gratitude of a good Scottish working woman, wrote a letter of thanks which was worded with such obvious sincerity that the donor of the bursary sought out the boy in school and promised to be responsible for his further education in the university.



At Glasgow Shearer went through his medical classes with uninterrupted success, supporting himself partly by working in his father's smithy and partly by playing football for St. Mirren. He often said that the golden sovereign which he received after a lost game, and the thirty shillings which rewarded a victory, were the greatest wealth he ever knew. After qualification he began to repay his debt at the rate of £2 a month, and carried out this duty faithfully for four years, when his benefactor, realising that he had made good beyond any shadow of doubt, gladly remitted the remaining amount.

Until the outbreak of war in 1914 Shearer was in general practice at Auchtermuchty. He gained in this busy rural practice that understanding of the conditions of work in a scattered country area which served him well in later years. The war brought for him, as for so many others, an uprooting and a long time of unsettlement. His service abroad was chiefly in Malta, where his buoyant health carried him through without serious illness.

Shortly after demobilisation he accepted, with great diffidence, a temporary post under the Highlands and Islands Medical Service, which is now merged in the Department of Health. He felt at the time that his lack of knowledge of the Highlands and his ignorance of Gaelic would be a serious hindrance to success. That it was not so was due to the fine qualities that he brought to his work—natural kindliness and humour, combined with an unusual ability to win affection. In an amazingly short period he learned the intricate geography of his area, and ultimately he became one of the greatest authorities on travel in the Highlands and Islands by land and sea and air. His racy tales of some of his winter hardships and of the atrocious conditions which Highland weather can produce were always listened to with wonder and eagerness. Those who knew Shearer will always remember him at his happiest moments, standing with bare head, in green Harris tweeds without an overcoat, chatting gaily with the captain of some little island steamer that was ploughing its way through tempestuous seas. Many of those who will miss him most are to be found in ships, in remote inns, and at desolate railway stations. His love of his fellow men extended far beyond his profession and his patients.

At the end of the fixed period Shearer's happiness was crowned by two events which expressed the professional, and the public, recognition of his life's work. On Feb. 2nd he read a paper to the Medico-Chirurgical Society of Edinburgh, in which he rendered his account of the Highlands and Islands Medical Service. In the course of the discussion which followed his remarkable exposition, Dr. John Orr summed up in a few phrases his life and work: "To-day we see the results of careful preparation by a man who seemed to be designed by nature to carry out this work, and I think that Scotland owes him a very great debt of gratitude." The second event which gave him great personal pleasure was the bestowal of the O.B.E., a decoration which he went to Buckingham Palace to receive within a few weeks of his death.

THE LATE MR. A. S. BARLING

AN obituary notice of Mr. Barling appeared last week. For the following appreciation we are indebted to Dr. J. A. Gibson:—

"Barling's retirement some years ago from the staff of the Royal Lancaster Infirmary, and a little later from consulting practice, was a serious loss to surgery in the district. His reputation was widespread; general practitioners in all parts of North Lancashire and Westmorland, even in Cumberland and the western districts of Yorkshire, were in the habit of sending to him their surgical cases for consultation and operation.

"As one who was for many years in constant association with him, assisting him at his operations or giving anæsthetics for him, I am enabled to appreciate his skill and personality. His accuracy in diagnosis, the result of experience, careful and acute observation, and reasoning which I must confess sometimes appeared to me to be uncanny, was again and again proved in the result. Like everyone else, he did make mistakes. But on the few occasions on which he seemed to go astray he was not infrequently misled by inaccurate or inadequate information, or in some cases allowed himself to be biased by previously expressed opinions.

"As an operator he was quick, neat, and efficient, and showed a ready resource and invention in dealing with unforeseen conditions and emergencies. He did like to talk while he was operating and appeared quite able to do so without his attention being distracted. He was not an easy man to assist, and could be very irascible when things were not going just quite right. His after-care of his patients was characterised by great attention to detail.

"As a man he was a delightful companion. In the early days before either of us owned a motor-car I spent many long hours in his company, travelling to visit and operate upon country patients. More

than once we had unusual and even exciting experiences in the wilds of Wyresdale, Dent, Hawes, and elsewhere. I still look back on these days as some of the most pleasant of my life, in spite of the discomforts sometimes experienced. He was a keen golfer for many years, and an excellent partner for a round; and, as well as being a capable yachtsman, he was an enthusiastic and successful amateur photographer. He had played rugby football in his youth, and retained a keen interest in this sport and also in cricket, more particularly if they were of Yorkshire vintage.

"He was a good talker, interested in a wide variety of subjects, an excellent host at his own evening fireside, a witty raconteur, and a good and ready speaker, especially excelling in the after-dinner variety. He was also a great reader and exhibited in his talk a wide and varied knowledge of English literature. Possibly his favourite authors were Shakespeare and Kipling, and having a very retentive memory, he would frequently regale his company with extracts, scenes, and episodes from their works. I have the happiest recollections of many hours spent with him abroad and at his home."

PUBLIC HEALTH

Medicine and Industry

THE report of the chief inspector of factories[1] contains much evidence that medicine can do more for industry than it does at present.

The work of the eleven medical inspectors, reviewed by Dr. J. C. Bridge in his chapter on Health, is impressive in its extent and its specialised variety. During 1937 they dealt with 685 cases of notified "poisonings," together with 196 reported cases of gassing. They studied 129 fatal cases of silicosis or silico-tuberculosis and 13 cases of asbestosis or asbesto-tuberculosis; furthermore, every case of suspected silicosis that is brought to the notice of the Department is carefully investigated. Nearly 2000 cases of dermatitis were voluntarily notified. The medical staff also continued their inquiries into the effects of the use of pneumatic tools and into the precautions to be taken during the use of radioactive substances in luminous paints. Remembering the wide areas of their districts (which cover the whole of England, Scotland, and Wales) and the necessary detailed routine work involved in the administration of the Factory Acts, it is obvious that the medical inspectors have much to keep in mind; and in addition we read of heavy duties in connexion with the new Factory Act, of attendances at conferences, on committees, and at public and private inquiries, any or all of which may involve elaborate preparation. The report states that it is proposed to increase the total numbers of factory inspectors from 290 to 332, and it would be a pity if any shortage of staff were to prevent the medical inspectorate from continuing to make the most of its great opportunities.

Dr. Bridge points out that industry is slowly making more use of medical knowledge; but is it making enough use of doctors? Unfortunately the industrial safety movement has grown up in isolation from the industrial health movement, and accident prevention has been too much the preserve of the industrial engineer. None would belittle the achievements of the engineers in this field, but we wonder whether a further contribution might not be made, for example, by a medical inspector dealing exclusively with the medical aspects of accidental injuries. There are three types of accident: those due to mechanical faults, those due to personal faults, and those due to "Acts of God." The vast majority of reported accidents are attributed to causes that are predominantly "personal." Thus accidents from hand tools, falling bodies, persons falling or stepping on or striking against objects or handling goods were responsible, between them, for no fewer than 125,000 of about 193,000 reported accidents. These are types of accidents which, as Mr. Thomas says, "legislation can hardly affect." The accident problem is becoming a personal problem. For example: "A foreman started up a machine without warning, though he knew that men were working on it"; "a man repairing a machine gave the signal for it to be restarted while he was in a dangerous position"; "a man was repairing a loom and set it in motion without first making sure that the weaver was clear." These personal failures accounted for 3 of the 1003 deaths recorded, and such failures often have a medical side. Every "accident," severe or trivial, presents a prima-facie case for investigation by someone qualified to detect the physical, psychological, or social causes at the back of it, and no coherent progress in accident prevention can be made unless emphasis is placed on the reasons why a workman loses interest in the safety of himself or others. It is easy to blame him, but it is more valuable to understand him. In the same way "labour-turnover" is partly a medical problem, and some years ago investigators of the Industrial Health Research Board were able to show that there is a positive correlation between sickness and accident liability.

The third chapter of the report deals with accidents to young persons, and here of course the same lessons emerge. A special study begun by the inspectors in 1937 was continued in 1938, and three tentative conclusions reached in 1937 were further confirmed: (1) that insufficient training is being given to young persons; (2) that among the personally caused accidents "some circumstances outside the factory should be considered"; and (3) that the statutory first-aid requirements alone are inadequate to prevent accident disablement. Training and instruction are the direct responsibility (under management) of the safety engineer or officer, but the other two aspects of accident prevention are largely medical. "Welfare" alone must prove to be inadequate because the situation can be dealt with only by accurate and painstaking diagnosis of the personal and group causes of accident-proneness.

Again we read that some juvenile accidents could be "attributed to the fact that the youngster was not equal to the work. . . . In many cases the work was not such that a young person under 18 years of age could normally be expected to perform with safety." If cases of this kind occurred in boys and girls under the age of 16, the examining surgeon would not be devoid of responsibility; but over that age, in most factories where an industrial medical officer is not employed, there is no doctor to decide whether the strength of the young person is a match for his work.

If the provision of a medical service is necessary for preventing accidents it is even more necessary for preventing industrial toxæmias and poisoning. Dr.

[1] Annual Report of the Chief Inspector of Factories and Workshops for the year 1937. Cmd. 5802. H.M. Stationery Office. 2s. (A preliminary review appeared in THE LANCET of August 13th, p. 384.)

Bridge leaves, in fact, no room for doubt about the necessity for more extensive and intensive medical work in industry. The new Act gives the Minister the power to require reasonable arrangements for medical supervision under certain circumstances. Will high accident-rates be considered to be "cases of illness" or "risks of injury to health" within the meaning of the Act? However that may be, power is now taken to require medical supervision where illness appears to be due to the nature of the work or to the introduction of new processes or substances. As Dr. Bridge says, "each year shows an increasing interest in the effect of industry on the health of the workers, and with that interest comes an effort to correlate ill-health with specific employment." It is not enough to prevent recognised industrial poisonings, nor to be able to foretell the effects on health of "the introduction of a new process or a new substance"; it is necessary also to learn to recognise and prevent the strictly occupational causes of so-called general illness such as "respiratory and gastric disorders."

Poliomyelitis

Newspaper reports emphasise the present incidence of poliomyelitis in particular communities—such as Braintree, where there have been 34 cases—and in particular families. For example, three children in one family at Felstead have contracted the disease (one having died) and others affected include their cousins. Two relatives of this family, it is stated, were employed in the house at Felsted School where four boys recovering from poliomyelitis were in residence. Again, all four cases reported on Tuesday last from Colchester came from a single family at Aldham. In two the diagnosis was definite, but the other two were only under suspicion.

A survey of the notifications gives a rather different impression: there are certainly local foci, but there is no large outbreak anywhere, and poliomyelitis is being reported from a great many different places. Thus during the week ended August 6th the 61 cases were notified from eighteen counties:

Bedford, 2 (Luton); Berkshire, 2 (Reading, Easthampstead R.D.); Cornwall, 1 (St. Austell R.D.); Cumberland, 1 (Maryport U.D.); Derby, 1 (Ripley U.D.); Essex, 16 (Braintree U.D. 8, Dagenham U.D. 1, Halstead U.D. 1, Chelmsford R.D. 1, Halstead R.D. 5); Herts, 1 (Barnet R.D.); Leicester, 1 (Lutterworth R.D.); Lincoln (Lindsey), 10 (Grimsby 6, Cleethorpes 3, Mablethorpe U.D. 1); London, 3 (Islington, Poplar, Woolwich); Salop, 1 (Wellington R.D.); Suffolk East, 1 (Ipswich); Surrey, 4 (Beddington 1, Farnham U.D. 3); Sussex West, 4 (Worthing 2, Worthing R.D. 2); Yorks East Riding, 2 (Hull); Carmarthen, 4 (Kidwelly 1, Carmarthen R.D. 3); Glamorgan, 6 (Swansea); Lancashire, 3 (Urmston U.D.).

Statements by medical officers of health and others convey the reassurance that in this country the disease is usually commonest towards the end of summer, that the present figures are only a little above the average for the time of year, and that most cases recover completely.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED AUGUST 6TH, 1938

Notifications.—The following cases of infectious disease were notified during the week: Small-pox, 3 (Lancs, Urmston U.D.); scarlet fever, 1248; diphtheria, 825; enteric fever, 49 (59 "expected"); pneumonia (primary or influenzal), 423; puerperal pyrexia, 181; cerebro-spinal fever, 13; acute poliomyelitis, 61; acute polio-encephalitis, 2; encephalitis lethargica, 2; dysentery, 19; ophthalmia neonatorum, 134. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on August 12th was 2845, which included: Scarlet fever, 570; diphtheria, 960 (carriers, 34); measles, 244; whooping-cough, 272; puerperal fever, 11 mothers (plus 5 babies); encephalitis lethargica, 277; poliomyelitis, 6. At St. Margaret's Hospital there were 28 babies (plus 11 mothers) with ophthalmia neonatorum.

Deaths.—In 126 great towns, including London, there was no death from small-pox, 2 (0) from enteric fever, 3 (0) from measles, 2 (1) from scarlet fever, 5 (0) from whooping-cough, 16 (0) from diphtheria, 34 (9) from diarrhœa and enteritis under two years, and 13 (4) from influenza. The figures in parentheses are those for London itself.

West Ham and Hull each reported a death from typhoid. Fatal cases of diphtheria occurred in 13 great towns, Manchester, South Shields, and Norwich each reporting 2. Birmingham had 3 deaths from diarrhœa.

The number of stillbirths notified during the week was 258 (corresponding to a rate of 42 per 1000 total births), including 46 in London.

MEDICAL NEWS

University of London

Applications are invited for the William Julius Mickle fellowship of the value of at least £200, which will be awarded by the senate to the graduate of the university, resident in London, who has done most to advance medical art or science within the last five years.

A Paul Philip Reitlinger prize of £30 will be awarded for the best essay embodying the result of some medical research carried out by the candidate. Candidates must be matriculated students who on June 1st preceding the award were studying in one of the medical schools of the university, or graduates of the university of not more than five years' standing. Regulations for the prize may be obtained from the academic registrar.

Applications are also invited for the Geoffrey E. Duveen travelling studentship of the value of £450, for research in any aspect of otorhinolaryngology. Candidates must be registered as medical practitioners or have had previous education and experience which in the opinion of the studentship board qualifies them to undertake such research. The studentship is normally tenable for one year, part of which shall be spent abroad, but it may be extended for six months or for one or two years. Forms of application may be obtained from the academic registrar.

Queen's University, Belfast

Applications are invited for the John Dunville research fellowship in experimental pathology at an annual salary of £500 and normally tenable for three years at the university. Further information may be obtained from the secretary.

Ross Institute of Tropical Hygiene

Dr. G. Macdonald, at present medical officer in charge of the Ross Institute branch in Ceylon, which is administered by a committee of the Ceylon Estates Proprietary Association, has been appointed assistant director of the Ross Institute (London School of Hygiene and Tropical Medicine) and will return to London from Ceylon at the end of the year to assist Sir Malcolm Watson in London. Dr. Robert Svensson will succeed Dr. Macdonald in Ceylon and Dr. J. W. Foster will take charge of a new branch in the Gold Coast at the end of the year. Dr. Svensson and Dr. Foster have both been appointed assistant directors of the Institute and before taking up their appointments they are making a tour of Bengal, Assam, Burma, and Malaya.

Dr. A. J. R. O'Brien has become a member of the standing committee in succession to the late Sir Thomas Stanton.

Appointments

BRADBROOKE, H. N., D.M. Oxon., M.R.C.P. Lond., Second Assistant Medical Officer to the County and City Mental Hospital, Oxford.

CHARLES, H. A., F.R.C.S. Eng., Registrar at the General Lying-in Hospital, Lambeth.

GORMAN, JAMES, M.B. Edin., D.P.H., Medical Officer of Health for Stalybridge.

MAYOU, C. R., M.R.C.S. Eng., Assistant School Medical Officer and Assistant Medical Officer of Health for Coventry.

RAFTERY, LILIAN, M.R.C.S. Eng., Resident Medical Officer and House Physician at the Elizabeth Garrett Anderson Hospital.

*WILLIAMS, J. J., L.R.C.P.I., Resident Assistant Medical Officer (Grade II) at the Crumpsall Hospital.

* Subject to confirmation.

Medical Referees under the Workmen's Compensation Act, 1925: Dr. E. W. M. H. PHILLIPS of Port Talbot, for the Neath and Port Talbot County Court District (Circuit No. 30); Dr. W. E. REES of Swansea, for Circuits Nos. 30 and 31; and Dr. L. G. R. ROBERTS of Leigh, for the Wigan (Circuit No. 6), Altrincham; and Warrington (Circuit No. 7) and Leigh (Circuit No. 8) County Court Districts.

Vacancies

For further information refer to the advertisement columns

Aberdeen Royal Infirmary.—Gynæcological Registrar.
Bedford County Hosp.—Second H.S., at rate of £150.
Birmingham and Midland Eye Hosp.—Res. Surg. O., £200.
Birmingham City, Rubery Hill and Hollymoor Division.—Jun. Asst. M.O., £350.
Boston General Hosp.—Res. M.O., at rate of £150.
Bradford City.—Asst. School M.O., £750.
Bristol Eye Hosp.—Jun. H.S., at rate of £100.
Bristol Royal Infirmary.—H.P., at rate of £80.
British Postgraduate Medical School, Ducane-road, W.—Res. Anæsthetist, and two H.S.'s, at rate of £150 and £105 respectively.
Burnley, Victoria Hosp.—H.P., at rate of £150.
Cardiff, King Edward VII Welsh National Memorial Association. Two Asst. Res. M.O.'s for Glan Ely Hosp., each £200.
Cardiff Royal Infirmary.—Res. M.O., £200.
Central London Ophthalmic Hosp., St. Pancras, W.C.—Sen. and Jun. H.S.'s, £120 and £100 respectively.
Chesterfield and North Derbyshire Royal Hosp.—H.S. to Ophth. and Ear, Nose, and Throat Depts., at rate of £150.
Chichester, Royal West Sussex Hosp.—Sen. H.S., £175.
Derby, Derbyshire Royal Infirmary.—H.S. for General Surgery, £150.
Derbyshire County Council.—Asst. Maternity and Child Welfare M.O., £600.
Derbyshire Education Committee.—Asst. School M.O., £500.
Douglas, Noble's Isle of Man Hosp. and Dispensary.—Res. H.S., £250.
Eastbourne Royal Eye Hosp., Pevensey-road.—H.S., at rate of £100.
Epsom County Hosp.—First Asst. M.O., £350.
General Lying-in Hosp., York road, S.E.—Jun. Res. M.O. and Anæsthetist, at rate of £100.
Glasgow, Lightburn Joint Hosp., Shettleston.—Res. Physician, £350.
Glasgow University.—Barclay Lectureship in Surgery and Orthopædics, &c., at Royal Hospital for Sick Children, £700.
Grimsby and District Hosp.—Res. Orthopædic Officer, £225.
Guy's Hosp., S.E.—M.O. for Dept. of V.D., £350.
Halifax General Hosp.—Jun. Res. M.O., £250.
Hastings, Royal East Hosp.—Hon. Surgeon and Hon. Asst. Surgeon.
Hertford County Hosp.—H.P., at rate of £150.
Hosp. for Sick Children, Great Ormond-street, W.C.—Eunice Oakes Research Fellowship, £700.
Hull, Anlaby-road Institution.—Asst. M.O., £350.
Hull Royal Infirmary.—H.P. to Sutton Branch Hosp., at rate of £160.
Ipswich, East Suffolk and Ipswich Hosp.—Cas. O., £144.
Kelling Sanatorium, Holt, Norfolk.—Med. Supt., £800.
Kent Education Committee.—Asst. School M.O. (Ophthalmic), £700.
Lancaster Royal Infirmary.—Sen. H.S., at rate of £200. Also Second H.S., at rate of £175.
Leamington Spa, Warneford General Hosp.—H.P., at rate of £150.
Liphook, Hants, King George's Sanatorium for Sailors.—Asst. M.O., at rate of £200.
Liverpool, City Infectious Diseases Hosps.—Asst. Res. M.O., £250.
London University.—University Chair of Radiology tenable at Royal Cancer Hospital, £2000.
Manchester and Salford Hosp. for Skin Diseases.—H.S., at rate of £150.
Manchester, Crumpsall Hosp.—Res. Asst. M.O., at rate of £200.
Manchester, Prestwich Mental Hosp.—Locum Tenens M.O., 7 guineas per week.
Manchester, St. Mary's Hosp.—Hon. Anæsthetist.
Manchester Ear Hosp., Grosvenor-square.—H.S., and Res. H.S., at rate of £150 and £120 respectively.
Manchester Northern Hosp., Cheetham Hill-road.—Res. Surg. O., £150.
Manchester Royal Eye Hosp.—Jun. H.S., £120.
Manchester Royal Infirmary.—Second Res. Clin. Pathologist, £150.
Mansfield and District General Hosp.—H.S., at rate of £150.
Melbourne, Women's Hosp.—Pathologist, £1000.
Middlesbrough, North Riding Infirmary.—Sen. H. S., £175.
Middlesbrough Education Committee.—Sen. Asst. School M.O., £500.
Monmouthshire County Council.—Assistant M.O., £500.
National Temperance Hosp., Hampstead-road, N.W.—Res. M.O., at rate of £175. Also Cas. O. and H.S., at rate of £120 and £100 respectively.
Nelson Hosp., Merton, S.W.—Res. H. S., at rate of £150.
Newcastle General Hosp.—Asst. Radiologist in charge of Deep Therapy Dept., £600.
Newcastle-upon-Tyne, Barrasford Sanatorium.—Res. Med. Asst., £250.
Newport, Mon., Royal Gwent Hosp.—Cas. O., £135.
Norwich, Jenny Lind Hosp. for Children.—Res. M.O., £120.
Oldham Royal Infirmary.—Two H.S.'s, each at rate of £175.
Oxford, Radcliffe Infirmary.—Hon. Physician to Dept. of Physical Medicine.
Plymouth, Prince of Wales's Hosp., Greenbank-road.—Two H.S.'s., and Res. Anæsthetist and H.S., each at rate of £120.
Plymouth, Prince of Wales's Hosp., Lockyer-street.—H.S., at rate of £150.
Preston, Biddulph Grange Orthopædic Hosp.—Jun. H.S., at rate of £200.
Prince of Wales's General Hosp., Tottenham, N.—Res. Jun. H.P. and two Res. Jun. H.S.'s, each at rate of £90.
Princess Elizabeth of York Hosp. for Children, Shadwell, E.—H.S., at rate of £125.
Queen Mary's Hosp. for the East End, Stratford, E.—Res. M.O's. each at rate of £150. Also Obstet. H.S., at rate of £110.
Reading, Royal Berkshire Hosp.—Res. M.O. for Blagrave Branch Hospital, at rate of £150.
Rochdale Infirmary and Dispensary.—Sen. H.S., £250.
Rotherham, Alma-road Hosp.—Deputy Med. Supt. and Obstet. Officer, £750. Also Asst. Res. M.O., £350.
Rotherham, Oakwood Hall Sanatorium.—Asst. M.O., £300.
Rotherham Hosp.—Cas. H.S., £150.
Royal Air Force.—M.O.'s.
Royal Eye Hosp., St. George's Circus, S.E.—Sen. H.S., and two H.S.'s, at rate of £150 and £100 respectively.
Royal Free Hosp., Gray's Inn-road, W.C.—Res. Cas. O., at rate of £150.
Royal London Ophthalmic Hosp., City-road, E.C.—Registrar, £200.
Royal Masonic Hosp., Ravenscourt Park, W.—Res. Surg. O., at rate of £250.
Royal Naval Medical Service.—M.O.'s.
Royal Northern Hosp., Holloway, N.—Med. Reg., £200.
Ryde, Royal Isle of Wight County Hosp.—H.S., £140. Also H.P., £130.
St. Helens Hosp., Lancs.—Jun. H.S., £150.
St. Mary's Hosp., W.—Med. Reg., £200.
St. Pancras Borough Council.—M.O.'s, each 1½ guineas per session.
Salisbury General Infirmary.—H.S., at rate of £125.
Sheffield, Children's Hosp.—H.P., at rate of £100.
Shrewsbury, Royal Salop Infirmary.—Res. Surg. O., £250.
Southampton, Royal South Hants and Southampton Hosp.—Res. Anæsthetist, at rate of £150.
Southend Municipal Hosp.—Asst. M.O., £325.
Southend-on-Sea General Hosp.—R.M.O. and Med. Reg., £300. Also Res. Anæsthetist and H.S., at rate of £125 and £100 respectively.
Stafford, Staffordshire General Infirmary.—Hon. Anæsthetist. Also Hon. Consulting Psychiatrist.
Tunbridge Wells, Kent and Sussex Hosp.—H.S., £150.
Union of South Africa, Trafalgar-square, W.C.—Sen. Prof. Officer (Physiology) and Sen. Prof. Officer (Bio-Chemistry), each £700.
Ventnor, Isle of Wight, Royal National Hosp. for Consumption, &c.—Second Asst. Res. M.O., at rate of £200.
Wanstead, Essex County Hosp.—M.O., £500.
West Ham Hosp. for Nervous and Mental Disorders, Goodmayes.—Jun. Asst. M.O., £350.
West Riding of Yorkshire County Council.—Asst. Tuber O., £500.
Wigan, Royal Albert Infirmary and Dispensary.—Hon. Asst. Surgeon, Res. Med. and Surg. O., and Reg., £250. Also H.S., at rate of £150.
Windsor, King Edward VII Hosp.—H.S., £120. Also Res. Surg. O.
Wolverhampton, New Cross Hosp.—Res. Asst. M.O., £200.
Worthing Hosp.—H.S. and H.P., each at rate of £130.

Medical Referee under the Workmen's Compensation Act, 1925, for the Reading, Chipping Norton, Oxford, Thame, Wallingford, Wantage, and Witney County Court Districts (Circuit No. 36). Applications should be addressed to the Private Secretary, Home Office, Whitehall, London, S.W.1, before Sept. 6th.

INSTRUCTION FOR THE D.P.H.—A three-months course of lectures and demonstrations on clinical practice and hospital administration will be given at the Brook Hospital, Shooter's Hill, Woolwich, S.E., by Dr. J. V. Armstrong, the medical superintendent, on Mondays and Wednesdays at 10.30 A.M., and alternate Saturdays at a time to be arranged, beginning Monday, Oct. 3rd, 1938. Applications should be addressed to the medical officer of health, London County Council, County Hall, S.E.1.

NOTES, COMMENTS, AND ABSTRACTS

ON CURRENT BRITISH TEACHING ABOUT NORMAL LABOUR AND ITS MANAGEMENT

By R. K. Howat, M.B., F.R.F.P.S. Glasg., F.R.C.S. Eng.

The aversion from pregnancy common among women to-day is often attributed to fear of death in childbirth. The fact that the rate of maternal deaths in labour continues almost undiminished despite modern methods of treatment suggests doubt of the efficacy of these methods. These considerations led to an inquiry into present-day British teaching about "normal" labour and its management as set out in sixteen text-books and manuals—English, Irish, and Scottish—published between 1929 and 1938.* The result is to disclose a state of affairs that excites misgiving.

Labour is unique among normal evacuatory functions in that when naturally performed it always causes suffering, often leads to considerable tissue damage, and so calls for treatment or management accordingly.

Variety of teaching is a good thing when it expresses the differences between active minds inquiring into unsolved problems, and rests upon recognition of basal facts. It is bad when there are gross discrepancies about anatomical facts, wrong statements about obvious phenomena, or dogmatic assertions resting on inadequate evidence or none at all. It is not good that nature's arrangements and methods for the normal discharge of a natural function should be in large measure ignored, distrusted, and in some particulars thwarted, in every case, no matter how normal and natural its condition and progress may be. Yet such is the effect of current British teaching as published. This is not due to lack of material for study, the supply of which has been constant and copious from time immemorial. The explanation lies elsewhere.

ANATOMICAL

The perineum.—In anatomy the perineum is described as including the tissues in front of the tip of the coccyx. In midwifery the term is restricted to the tissues from the anus to the vaginal opening. Yet in a number of books this is left to be inferred instead of being expressly stated. But for this inference some of their teachings would be so mutually contradictory as to be incomprehensible. One teacher, at least, does indeed say that the perineum lies "between the posterior fourchette and the anus." [10] He also says that it consists of skin only, whereas other teachers refer to perineal muscles, which accords with the ordinary description of the perineum. Reconciliation between these differing descriptions of anatomical structure would appear to be difficult.

The child's head.—Scottish teaching [12 13] correctly refers to the posterior end of the suboccipito-bregmatic diameter as a point, and locates it midway between the external occipital protuberance and the foramen magnum, a site concealed in the flesh-clad head of the living child. Irish teaching [10] locates it at "the point where the head joins the back of the neck below the occipital prominence," a doubly ambiguous location since the head does not join the back of the neck at a point, and this "prominence" varies with the position of the head. In the anatomical position it is, in the adult, about an inch above the external occipital protuberance; in the fully flexed head it is the protuberance itself. English teaching [3 18] seems to bear equally little relation to the meaning of the word "diameter." It locates the point at "the junction of the head and neck behind." This junction occupies that large area of the occipital bone between the superior nuchal lines and the foramen magnum. Anything less like a point it would be hard to imagine.

The length of the suboccipito-bregmatic circumference is variously stated at from 11 in. [12 19] to 13 in. [6] No explanation of such a great difference is offered. That individual heads so differ is doubtless true. That *average* measurements, if widely enough based, thus differ is incredible.

In at least two books [6 10] the normal mechanism of vertex presentations is described with reference to diameters, not circumferences, of the fœtal head. No mention is made of the latter although these, not the diameters, are the factors which decide the degree of stretching which the maternal parts must undergo.

FIRST STAGE OF LABOUR

Perineal distensibility differs in different cases over a wide range, from the healthy young woman with succulent flesh and copious secretion to the middle-aged primipara, spare and withered, with dry and inelastic tissues. These extreme types illustrate the Scottish midwives' saying "A greasy labour is an easy labour, but a dry ane's aye dreich." That the distensibility of a rigid perineum may be modified by hot fomentations is passingly mentioned by a few teachers, by some of them [1] with qualified approval, by others [3 18] with sceptic disbelief. Unmentioned is the more potent old-fashioned hip or sitz bath used as hot as can be borne, in which the quantity and the temperature of the water can be varied without disturbing the patient. This flushes the pelvic parts with blood, softens the perineal tissues, and promotes secretion.

SECOND STAGE OF LABOUR

State of the pelvic floor muscles.—That these muscles are contracted during the pains of the second stage is exclusively Scottish teaching, product of the Edinburgh [12 14] and Glasgow [13] schools. These muscles are variously described as "tightly contracted," [12] "rather contracted," [13] and "contracted rather than relaxed," [14] whatever that means. As a fact they are neither contracted nor relaxed; on the contrary they are tensely stretched. These "rather" half-hearted statements might be thought to hint at some doubt of their correctness in the writers' minds were it not that the teaching has been put forward for years. No grounds are offered, not a tittle of evidence is advanced, for this teaching which contradicts the manifest phenomena of labour. It is precisely during the pains that the vaginal and anal orifices and their embracing sphincters are more and more stretched; that the downward dome-like stretching of the perineum and its muscles (levatores ani and transverse perineal), occurs; and that the levators are also stretched outwards through their being forced apart by the transverse diameter of the emerging head.

It may be that the error is due to mistaking tension for contraction. During the pains the muscles are tense indeed, not seldom to rupture point. But if

* A numbered list of these books is given at the end of this article. The references in the text are merely illustrative and confirmatory, not exhaustive.

this be the explanation it is remarkable that this mistaken teaching should be proferred by quite a number of teachers connected with two of our largest schools; it is surprising that it should be persisted in—it is over eleven years since it was shown to be wrong [8]; and it is very surprising and disturbing to find that so obvious a mistake should have been made at all by leading obstetricians.

Rate of delivery.—Teaching is unanimous that delivery must not be "too rapid," that it must be slow enough to allow time for the perineum to distend to its utmost. To effect this various manœuvres are advocated, of which the simplest seems to be manual resistance applied to the exposed part of the child's head. With experience, doubtless, a sense of the practical meaning of these terms comes to be acquired; but beginners will search the books in vain for any pointer, any actual measure of guidance to what teachers exactly mean by these words. It is here submitted that an adequate rate of advance is one that allows an additional ¼–½ in. of sagittal-line scalp to escape from the vagina at every pain, the smaller figure applying as crowning is closely approached, and that restraint of the head is not called for before the anus has begun to dilate, and unless this rate of advance be exceeded.

In the absence of precipitate labour perineal rupture, if it occur, is usually "inevitable." Its imminence is indicated by the tense anterior perineum appearing pale and glistening. Its extent can be readily limited by cross-section of the perineum.[9]

Maintenance of cranial flexion.—With one apparent exception [14] all the teachers reviewed agree that in every case, in order to lessen the risk of perineal rupture, flexion of the head should be maintained and extension resisted until the head has so far descended as to bring, not the occiput, but the nape of the neck under the pubic arch, and thus to ensure that the suboccipito-frontal plane of the head will be the largest to occupy the vaginal outlet. One teacher [2] writes that "in the vast majority of cases if left alone . . . flexion . . . will be kept up until the nape of the neck is hitched beneath the symphysis"—a majority estimated by others [11] at "probably 90 per cent." If this teaching be true then it follows that in the vast majority (probably 90 per cent.) of cases the interference advocated is superfluous. Why the exceptional cases (probably 10 per cent.) should not be recognised and dealt with if and when they occur is not explained. On this point the books are silent.

The teaching [3] indicates that there are two alternatives—namely, (1) arrest of the occiput under the symphysis and consequent distension of the vaginal outlet by the occipito-frontal plane of the child's head, and (2) arrest of the nape of the neck under the symphysis and consequent distension of the outlet by the suboccipito-frontal plane—and that the relative risks of perineal rupture correspond to and depend upon the girths of these planes. Actually the position is less simple. Because the nape of the neck is a wider and (anatomically) a lower part of the body than the occipital pole its engagement under the symphysis requires a farther descent of the child's head, with consequent further stretching of the perineum, and a correspondingly greater risk of rupture. Thus the alternatives really are (1) less descent with larger plane, and (2) more descent with smaller plane. Each of these alternatives thus consists of two mutually conflicting factors.

Published teaching makes no mention of the effect of these different degrees of descent of the head and of the risks of rupture that they involve. No estimate of the *resultant* risks (the crucial matter) is given. To ignore one factor in the situation and its effect, to apply this defective measure to 10 per cent. of all cases, and, on the strength of the supposed result, to teach that therefore there should be in all cases (100 per cent.) active interference with the normal discharge of a natural function is not calculated to carry conviction. The actual position seems to be that teaching, as published, has not measured and considered all the factors involved; that that teaching is put forward as conclusive, whereas it is, in part at least, speculative; that it *may* be right; that its advocates have not proved it so; and that it may be mistaken.

Delivery of the head between pains.—Akin to the foregoing instances of meddlesome midwifery is the unanimous teaching that the head should never be allowed to be born naturally during a pain, but should always be delivered artificially between pains. The methods recommended for this purpose are very various. Some teachers advocate pressure upon the head with a swab,[15] the palm,[14] the heel of the hand,[10] behind the anus; others [16] with the fingers beside the anus; some do not say how the pressure that they advocate is to be applied. (Pressure with the fingers *in* the anus, formerly recommended, seems now out of favour.) Some [7] advise pressure on the perineum; others [12 14] condemn this. Some [2 13 14] teach that pressure should be made between the anus and the coccyx upon the frontal region of the head; others [15 19] that one should press at this site on the child's chin. How the child's brow and chin can be in the same place at the same stage is not explained. Some [10] advise pulling the head forward with the fingers applied to the exposed scalp, but do not say how they are to get a hold on the smooth slimy surface. Some [6 7] teach that the perineum should be pushed or pulled back over the head; others [12 14] condemn this. How it can be done without increasing the risk of rupture anyone who has tried it on a tensely stretched perineum may well wonder. Localised finger pressure at one or more points on a tense thin perineal margin is more conducive to rupture than is the evenly distributed pressure of the globular advancing head.

If it be true, as is taught, that the head's advance can be controlled by manual pressure on the exposed scalp and perineal integrity be thus favoured, why should delivery between pains be attempted at all? For their teaching that the head should be so delivered some writers [6 18 19] give no explanatory reason at all. Scottish teachers [12 13 14] explain that by delivering between pains one avoids that contraction of the pelvic floor muscles which (they say) occurs during the pains. But this teaching has been shown years ago [8] to be erroneous, the pelvic floor and its muscles being stretched, not contracted. The reason usually suggested in the books is that between pains the head can be delivered through relaxed parts. This teaching is little less mistaken than the other. A small head can, indeed, be so delivered, and equally easily can be born naturally—i.e., during a pain—without risk of rupture from its size. But if the head and the pelvis be of average size then the head *cannot* be delivered through relaxed tissues. Under these conditions the pelvic floor will be tightly stretched whether delivery be effected by nature during pains or by hand between pains, for the method of delivery does not alter either the size of the head or the consistence and quality of the perineal flesh. No convincing reason is offered for this advised interference with natural delivery.

Ironing the perineum is a method of distending the perineum commended in American books. It consists in introducing the entire hand within the vagina, closing it there, and withdrawing it closed with the back of the hand against the posterior vaginal wall. Presumably the writers regard the fist as an acceptable, if not preferable, alternative to the globular head as a distending agent. Two Scottish books [12] [13] mention it in terms that leave it in doubt whether their authors regard the procedure as good or indifferent. Bad they presumably do not think it, since they suggest its use. English and Irish writers seem to indicate their opinion of it by ignoring the nasty thing.

THIRD STAGE OF LABOUR

Abdominal manipulation.—Not long ago very active manipulation of the uterus in the third stage was widely advocated, but this is now abandoned. That in the third stage of every normal labour there should be some "watching" manipulation of the abdominal wall seems to be agreed by all teachers save one.[15] He writes "After the baby is born . . . the attendant . . . should not touch the abdomen." The difference in the teaching may not be important, but it is interesting and refreshing to those of us who deplore the unnatural methods that characterise current teaching.

THE NATURAL FUNCTION

Nine years ago Jellett and Madill[11] wrote: "Labour under normal conditions is a physiological process; we cannot interfere with it without making it a pathological process, and introducing complications whose possibilities for harm are infinite; therefore the wise and skilful obstetrician avoids interference." Last year Jellett[10] wrote: "The whole management of normal labour may be summed up in a few words—to maintain the patient's strength, to relieve pain and lessen nerve strain, to help the natural efforts in a natural way, and to avoid meddlesome and dangerous interference. The more we depart from these principles, the greater is the morbidity and mortality amongst our patients, and yet, at the present time, certain teachers of midwifery, who should know better, openly teach methods which are in direct opposition to the fact that normal labour is a physiological process." Fine words, resounding phrases, scathing comment! Yet a cursory reading of the text in which they occur will suffice to show how widely the practice therein advised differs from the principles so definitely stated.

With teaching so copious, so various, so confusing, conflicting, and mistaken, choice is wide and perplexity almost inevitable unless that teaching be scrutinised with a sceptical detachment for which the need is abundantly plain. "Meddlesome midwifery," formerly a term of reproach for needless interference with the normal discharge of a natural function, seems to have lost that significance for present-day teachers, although it is an apt description of much of their teaching. The spirit and policy of that teaching are opposed to the watchful observation of nature and a readiness to intervene should her machinery work awry. Rather the attendant must dominate nature, be ever active, always doing something, at least in the later part of the second and all of the third stages of every labour. For the practitioner, trying to give effect to this and to attend to other calls upon his time, the result is apt to be, not a simple return to more natural methods, but a morbidly excessive activity conducive to mischiefs else avoided—hasty use of forceps, perineal rupture, post-partum hæmorrhage to wit. An instance of this is afforded by a doctor with a very large practice which included, he said, some four hundred confinements a year. He used to explain that he had trained the midwives and handy women who "followed" him to send for him when the head was on the perineum, and that he allowed himself twenty minutes to be "into the house, on with the tongs, out with the kid, and off in the car." That practice was unequalled as an individual source of perineorrhaphic material to the local hospital. How far the influence of "active" teaching extends in this way it is impossible to know.

Not only practice shows its effects. Equipment, too, is affected by it, more especially in America. One American professor [4] advises that for an ordinary domiciliary confinement the medical attendant should take with him to the patient's house an armamentarium (apt word) of over one hundred articles. This dwarfs anything of the kind in British teaching.

Their published writings go to show that British teachers of midwifery to-day, without exception, hold and teach not that normal parturition is a natural function to be naturally performed so long as it progresses normally, but that it is a process calling for active interference in every case; not that it is subject to complications which should be watched for and treated as and when they occur, but rather that in normal labour complications, not amenable to corrective treatment, arise so frequently that their advent should never be awaited, and that, irrespective of their degrees of probability, they should be anticipated by active interference in every case, no matter how "normal" its phenomena and progress may be. This is very remarkable teaching. It involves a very pretentious claim and requires of its advocates irresistibly convincing evidence in support to induce its satisfactory acceptance. No such evidence is provided in the books. That in these circumstances it is advocated by so many obstetricians occupying important and influential positions as teachers is disturbing; that it is associated with a practically undiminished maternal mortality is more disturbing. Whether this school of intensely active interference will prove to be lasting or will change to one of more conservative outlook remains to be seen. That the conditions have occasioned disappointment and anxiety may be recognised from both the professional and the lay press.

Current teaching contrasts with that of an earlier generation in its advocacy, in the management of normal labour, of two things in combination—namely, invariable and active interference in every case and the scrupulous observance of rigid surgical cleanliness. The first favours septic infection, a fruitful source of puerperal morbidity and mortality. The second combats it. Its employment in conjunction with a less meddlesome midwifery and a greater reliance upon nature's mechanism of delivery would be likely to yield improved results in respect of both disease and death. There seems no sufficient reason why it should not be widely tried, and strong reason why it should. Institutional midwifery can most quickly and readily yield a statistical estimate of its effects, and thus help to place "normal" midwifery on a more satisfactory footing and to lessen widespread dissatisfaction with the existing state of affairs.

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(*Continued at foot of next page*)

A NEW JOURNAL OF INDUSTRIAL DISEASES

THE study of industrial diseases is one of increasing importance, and an influential committee in France has decided to publish a journal devoted entirely to it. There are already other journals of industrial diseases, notably a German one, and a combined American and English publication. In the first volume of the French journal [1]—*Archives des Maladies Professionelles*—which has just reached us, the committee of direction, consisting of Profs. Balthazard, Duvoir, Fabre, Leclerq, and Mazel, say that the aim is to furnish, from an independent and scientific standpoint, all the available information about industrial diseases and poisonings. A feature of the journal will be a section containing abstracts of important articles appearing in French and foreign periodicals, and there will also be a classified bibliography of papers dealing with the various aspects of industrial diseases, workmen's compensation, and preventive medicine. It is hoped to publish a number of the journal containing 80 pages every two months.

In the first number Prof. V. Balthazard discusses the study and teaching of occupational diseases, and gives a brief outline of the legal measures adopted by France in dealing with workmen's compensation. These laws are characterised by the caution and restraint of the legislature in laying down which diseases or poisonings should be compensated. In comparison with the workmen's compensation Acts in other countries such caution might justifiably be called excessive, because in 1919 poisoning by lead and mercury were the only diseases on the compensation schedule. In 1931 poisoning by such substances as benzol and tetrachlorethane were added, and at the present time the list only contains 10 such items. Not only does parliament decide which poisonings shall be scheduled but it also sets forth the signs and symptoms which can be accepted for compensation. If a workman is suffering, say, from lead poisoning, but has atypical symptoms, he cannot receive compensation. In the discussion on lead poisoning, a deputy moved that the encephalopathies be omitted from the list of symptoms, saying: "You are going to compensate a painter each time he gets a headache." He had confused *encéphalopathie* with *céphalée*. But the encephalopathies were nevertheless omitted from the list of compensatable symptoms.

Prof. M. Duvoir deals with the rôle of the doctor in industry, and sketches the history of industrial medicine, paying particular attention to Ramazzini (1633–1714). His review would have been more complete if he had mentioned the important pioneer work carried out in the present century by, among others, Sir Thomas Legge in this country, and by Dr. Alice Hamilton in the United States of America. Prof. R. Fabre and E. Kahane contribute a paper entitled Introduction to the Biochemical Study of the Pneumoconioses and M. Kossanovitch of Belgrade describes the systems of social insurance and occupational diseases of Yugoslavia. The managing editor of the journal, M. Guy Hausser, makes a contribution to the question as to whether or not the distribution of milk to workers can prevent the onset of occupational diseases.

[1] *Archives des Maladies Professionelles, Hygiène et Toxicologie Industrielles.* Vol. I. No. 1. March–April, 1938. Paris: Masson et Cie.

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SAFETY IN CHEMICAL WORKS

THE Association of British Chemical Manufacturers has issued a revised edition of its model rules for safety in chemical works. The new pamphlet, which takes into account the Factories Act, 1937, only just in force, is well up to date. Most of the 117 rules set out seem obvious enough but every one of them has probably been broken again and again, sometimes with disastrous results. All laboratory workers must remember taking risks with no worse effect than an occasional flare-up or some slight damage to clothing. But when the material handled can be measured in kilogrammes or tons, rules and even penalties rather than recommendations are essential. Rule 6, which recommends the organisation of safety committees and membership of some external "safety association," is very sound if only because interchange of experiences may lead to the spread of knowledge of unexpected and perhaps unreported dangers. Rule 14, designed to reduce to a minimum the escape of products likely to give rise to fire or explosion, may save the life of men working in sewers. Rules 17 and 18 deal with electrical equipment and static charges. The mixing of effluents which may cause the evolution of poisonous gases seems a fertile cause of danger (Rule 47). Instruction is included on the dangerous properties of materials which workers may have to handle and of gases, fumes, or vapours that may be evolved; on measures to prevent poisoning; and on the possible effect of long exposure to low concentrations that cause no immediate harm or discomfort. The rule as to entry of enclosed plant only after isolation, ventilation, and testing, which must be recorded in a book, is one which if it had always been followed would have saved many lives. The precautions laid down for personal cleanliness, especially the emphasis laid on the need for bathing or washing after having been splashed with aniline or similar poisonous material which can be absorbed through the skin, deserve particular attention. The pamphlet is issued from the Association's office, 166, Piccadilly, London, W.1.

Births, Marriages, and Deaths

BIRTHS

BARRY.—On August 11th, at City-road, London, the wife of Surgeon-Comdr. T. L. Barry, R.N.—a son.

BEARD.—On August 14th, the wife of Dr. A. J. W. Beard, of Wimbledon—a son.

KEEBLE.—On August 10th, at Gerrard's Cross, the wife of Dr. E. R. Keeble—a son.

LITTLE.—On August 11th, 1938, at the Shearwood-road Nursing Home, Sheffield, to Megan, wife of George S. R. Little, M.R.C.S., L.R.C.P., of Worksop, Notts—a sister for David.

MACBETH.—On August 10th, at Oxford, the wife of Mr. Ronald G. Macbeth, F.R.C.S.—a daughter.

STEPHENS.—On August 12th, at Gidea Park, Essex, the wife of Dr. D. J. Stephens—a son.

WRIGHT.—On August 11th, at Nuffield House, S.E., the wife of Dr. G. Payling Wright—a son.

ENGAGEMENT

Major E. AINGER and Dr. K. W. DUNN-PATTISON.—The engagement is announced between Major Edward Ainger, late 3rd The King's Own Hussars, and Katherine Winifred Dunn-Pattison, M.B., younger daughter of the late Capt. R. P. Dunn-Pattison and of Mrs. Dunn-Pattison, of Wimbledon.

GOLDEN WEDDING

BATTEN—CONDER.—On August 14th, 1888, at East Parade Chapel, Leeds, Rayner Derry Batten, M.D. Lond., to Katharine Roubiliac Conder. Present address: 82, Campden Hill-road, W.8.

DEATHS

DIAS.—On August 7th, in Paris, Anthony Dias, M.R.C.S. Eng., late Anglo-Iranian Oil Co.

DICKINSON.—On August 14th, John Cuthbert George Dickinson, M.B. Lond., M.R.C.S. Eng., of Braunton, N. Devon.

JEREMY.—On August 16th, Harold Rowe Jeremy, F.R.C.S. Eng., of Harley-street, W.

MAXWELL.—On August 10th, at St. Leonards-on-Sea, Ernest James Maxwell, M.B. Camb.

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages, and Deaths.